STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 120504

To: Sarvamangala Devi **Location:** REM 3C18 **Art Unit:** 1645 Monday, May 03, 2004 **Case Serial Number:** 10/041775	**From:** Beverly Shears **Location:** Remsen Bldg. RM 1A54 **Phone:** 571-272-2528 beverly.shears@uspto.gov

Search Notes

Shears, Beverly

From: Devi, Sarvamangala
Sent: Monday, April 26, 2004 9:36 AM
To: Shears, Beverly
Subject: 10/041,775

Beverly:

Please perform a sequence and an interference search for SEQ ID NO: 2 in application SN 10/041,775.

Please include an inventors' name search; Inventors: Eric Brown; Lawrence Lee; and Magnus Hook

Please include a text search for the following claim(s):

Claim 1: A method of treating or preventing pathogenic conditions, such as, toxic shock syndrome and poison ivy, associated with overstimulation of T cells in a human or animal patient comprising administering an isolated Staphylococcus aureus Mapl9 protein, a 72 kDa protein which binds to extracellular matrix components.

Thanks.

S. DEVI, Ph.D.
AU 1645
Rems - 3C18

Date completed: 04-30-04
Searcher: Beverly c 2528
Terminal time: _____
Elapsed time: _____
CPU time: _____
Total time: _____
Number of Searches: _____
Number of Databases: 3

Search Site
_____ STIC
_____ CM-1
_____ Pre-S

Type of Search
_____ N.A. Sequence
_____ A.A. Sequence
_____ Structure
_____ Bibliographic

Vendors
_____ IG
✓ STN
✓ Dialog
_____ APS
_____ Geninfo
_____ SDC
_____ DARC/Questel
✓ Other CGN

STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 110017

To: Sarvamangala Devi **Location:** CM1/7E15 **Art Unit:** 1645 **Wednesday, December 10, 2003** **Case Serial Number:** 10/041775	**From:** E **Location:** I **Phone:** [redacted] beverly.shears@uspto.gov

Search Notes

Shears, Beverly

From: Devi, Sarvamangala
Sent: Tuesday, December 09, 2003 7:44 AM
To: Shears, Beverly
Subject: 10/041,775

Beverly:

In application 10/041,775, would you please perform a sequence and an interference search for SEQ ID NO: 2 and SEQ ID N: 4?

Thanks.

S. DEVI, Ph.D.
AU 1645
CM1-7E15

Date completed: _____	**Search Site**	**Vendors**
Searcher: Beverly 9994	_____ STIC	_____ IG
Terminal time: 23	_____ CM-1	_____ STN
Elapsed time: _____	_____ Pre-S	_____ Dialog
CPU time: _____	**Type of Search**	_____ APS
Total time: 25	_____ N.A. Sequence	_____ Geninfo
Number of Searches: _____	_____ A.A. Sequence	_____ SDC
Number of Databases: 1	_____ Structure	_____ DARC/Questel
	_____ Bibliographic	✓ Other CGN

PTO-1590 (9-90)

Devi, S.
10/041775

- Key terms

FILE 'REGISTRY' ENTERED AT 15:34:14 ON 30 APR 2004
E "ADHESIN MAP19"/CN 5
L1 1 S E4

FILE 'HCAPLUS' ENTERED AT 15:34:21 ON 30 APR 2004
L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON "ADHESIN MAP19 (STAPHYLOCOCCUS AUREUS)"/CN
L5 45 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 OR (MAP19 OR MAP 19 OR (MHC OR MAJOR(W)(HISTOCOMPAT? OR HISTO COMPAT?)(W)COMP LEX)(5A)((CLASS OR TYPE)(W)(II OR 2)) OR MHCII)(S)AUREUS
L6 16 SEA FILE=HCAPLUS ABB=ON PLU=ON L5 AND ((TOXIC OR SEPTIC OR ENDOTOXIC)(W)SHOCK OR POISON IVY OR TSS OR TOXICODENDRON OR TOXICO DENDRON OR (T(W)(CELL OR LYMPHOCYT?) OR PATHOGENIC?)(5A)(DISEAS? OR DISORDER OR CONDITION))

L6 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 20 May 2003
ACCESSION NUMBER: 2003:383694 HCAPLUS
DOCUMENT NUMBER: 139:190422
TITLE: Therapeutic approaches to superantigen-based diseases: A review
AUTHOR(S): Hong-Geller, Elizabeth; Gupta, Goutam
CORPORATE SOURCE: Biosciences Division, HRL-1, Los Alamos National Laboratory, Los Alamos, NM, 87545, USA
SOURCE: Journal of Molecular Recognition (2003), 16(2), 91-101
CODEN: JMORE4; ISSN: 0952-3499
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Superantigens secreted by the bacterial pathogen Staphyloccocus **aureus** are extremely potent toxins that overstimulate the host immune system by binding to the **MHC class II** and T cell receptors and activating a large population of T cells. Superantigen infection has been shown to be the causative agents in acute diseases, food poisoning, and **toxic shock** syndrome, and in more chronic conditions such as inflammatory skin diseases. In addition to the toll on public health, S. aureus superantigens also represent a potential biothreat to the national security. To address these risks, a number of different therapeutic strategies have been developed that target different aspects of the pathogenic mechanism of S. aureus and superantigen infection. These therapies, which encompass strategies as diverse as the production of neutralizing antibodies, inhibitory peptide/receptor design, and blockage of superantigen gene transcription, are being tested for treatment of established S. aureus infections in pre- and post-exposure scenarios. In this review, the authors describe these different strategies and their efficacies in inhibition of superantigen-induced effects in the host, and present the future outlook for successfully producing therapies for superantigen-based disease.
REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Searcher : Shears 571-272-2528

L6 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 28 Jan 2003
ACCESSION NUMBER: 2003:65811 HCAPLUS
DOCUMENT NUMBER: 138:319226
TITLE: Research on Superantigenic Toxins Integrating Bacteriology, Immunology, Bacterial Toxins, and Clinical Infections Diseases
AUTHOR(S): Uchiyama, Takehiko
CORPORATE SOURCE: Department of Microbiology and Immunology, Institute of Laboratory Animals, School of Medicine, Tokyo Women's Medical University, Japan
SOURCE: Nippon Saikingaku Zasshi (2002), 57(4), 563-579
CODEN: NSKZAM; ISSN: 0021-4930
PUBLISHER: Nippon Saikin Gakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review discusses toxins with superantigenic activity from bacteria. **Toxic shock** syndrome toxin-1 (TSST-1) from Staphylococcus **aureus** activates T lymphocyte through binding to **MHC class II** mols. SpeA (Streptococcal pyrogenic exotoxin A) ia also a toxin with superantigenic activity. YPM (Yersinia pseudotuberculosis-derived mitogen) is the causing toxin of Yersinia infection.

L6 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 26 Nov 2002
ACCESSION NUMBER: 2002:897499 HCAPLUS
DOCUMENT NUMBER: 138:3644
TITLE: The Staphylococcus aureus Map protein is an immunomodulator that interferes with T cell-mediated responses
AUTHOR(S): Lee, Lawrence Y.; Miyamoto, Yuko J.; McIntyre, Bradley W.; Hook, Magnus; McCrea, Kirk W.; McDevitt, Damien; Brown, Eric L.
CORPORATE SOURCE: The Center for Extracellular Matrix Biology, Albert B. Alkek Institute of Biosciences and Technology, Texas A and M University System Health Science Center, Houston, TX, 77030-7552, USA
SOURCE: Journal of Clinical Investigation (2002), 110(10), 1461-1471
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Staphylococcus aureus (SA) is an opportunistic pathogen that affects a variety of organ systems and is responsible for many diseases worldwide. SA express an MHC class II analog protein (Map), which may potentiate SA survival by modulating host immunity. The authors tested this hypothesis in mice by generating Map-deficient SA (Map-SA) and comparing disease outcome to wild-type Map-SA-infected mice. Map-SA-infected mice presented with significantly reduced levels of arthritis, osteomyelitis, and abscess formation compared with control animals. Furthermore, Map-SA-infected nude mice developed arthritis and osteomyelitis to a severity similar to

Map+SA-infected controls, suggesting that **T cells** can affect **disease** outcome following SA infection and Map may attenuate cellular immunity against SA. The capacity of Map to alter T cell function was tested more specifically in vitro and in vivo using native and recombinant forms of Map. T cells or mice treated with recombinant Map had reduced T cell proliferative responses and a significantly reduced delayed-type hypersensitivity response to challenge antigen, resp. These data suggest a role for Map as an immunomodulatory protein that may play a role in persistent SA infections by affecting protective cellular immunity.

REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 22 Oct 2002
ACCESSION NUMBER: 2002:801310 HCAPLUS
DOCUMENT NUMBER: 138:185995
TITLE: Epitope mapping of neutralizing TSST-1 specific antibodies induced by immunization with toxin or toxoids
AUTHOR(S): Gampfer, Jorg M.; Samstag, Aysen; Waclavicek, Martina; Wolf, Hermann M.; Eibl, Martha M.; Gulle, Heinz
CORPORATE SOURCE: Biomedizinische Forschungsgesellschaft mbH, Vienna, A-1090, Austria
SOURCE: Vaccine (2002), 20(31-32), 3675-3684
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Toxic shock** syndrome toxin-1 (TSST-1), a superantigen produced by Staphylococcus aureus, is a potent stimulator of the immune system. T-cells are activated by crosslinking of MHC class II mols. on antigen presenting cells with T-cell receptors (TCR). TSST-1 is associated with the majority of the cases of menstrual staphylococcal **toxic shock**, a severe and life-threatening multisystem disorder. Even though antibody mediated protection has been studied, information on antibody specificity directed to individual antigenic determinants of the protein is incomplete. To obtain immunogens with low toxicity, the authors generated a double-site mutant (dmTSST-1), modified at solvent-exposed residues predicted to be important for both **MHC class II** and TCR binding, and detoxified recombinantly expressed TSST-1 (rTSST-1) as well as native TSST-1 (nTSST-1) isolated from Staphylococcus **aureus** by treatment with formaldehyde. Rabbits were immunized with rTSST-1, nTSST-1, dmTSST-1, and formaldehyde inactivated toxoids. The sera obtained were used to map the antigen-reactive regions of the mol. and to identify specificities of antibodies induced by immunization with the different antigens. To detect linear antigenic epitopes of TSST-1 the reactivity of the sera with 11-meric peptides having an overhang of four residues, covering the entire mol. of TSST-1, have been studied. The authors found that sera of TSST-1 immunized rabbits predominantly reacted with N-terminal residues 1-15, while sera generated with formaldehyde

inactivated toxoid recognized a total of 7 regions located at the N- and C-terminus and internal sites of TSST-1. Despite different specificities all sera were able to inhibit TSST-1 induced proliferation of human mononuclear cells.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 04 Oct 2002
ACCESSION NUMBER: 2002:754410 HCAPLUS
DOCUMENT NUMBER: 137:277779
TITLE: Method of preventing T cell-mediated responses by the use of the **major histocompatibility complex class II** analog protein (Map protein) from Staphylococcus **aureus**
INVENTOR(S): Brown, Eric N.; Lee, Lawrence Y.; Hook, Magnus
PATENT ASSIGNEE(S): The Texas A & M University System, USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002077010	A2	20021003	WO 2002-US401	20020110
WO 2002077010	C2	20021114		
WO 2002077010	A3	20030403		
WO 2002077010	C1	20031113		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003108564	A1	20030612	US 2002-41775	20020110
EP 1355662	A2	20031029	EP 2002-736474	20020110

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 2001-260523P P 20010110
WO 2002-US401 W 20020110

AB A method of immunomodulating the T cell response in Staphylococcal bacteria is provided wherein an effective amount of the Map protein from Staphylococcus aureus is administered to a host to prevent or suppress the T cell response. The present method may be utilized with either the Map protein or an effective subdomain of a fragment thereof such as the Map10 or Map19 protein. The present invention is advantageous in that suppression or prevention of the T cell

response in a host can prevent or ameliorate a wide variety of the **pathogenic conditions** such as **T cell** lymphoproliferative **disease** and **toxic shock** syndrome wherein the overstimulation of T cell needs to be suppressed or modulated.

IT **466134-40-7**, Adhesin **Map19** (Staphylococcus **aureus**)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; method of preventing T cell-mediated responses by the use of the **major histocompatibility complex class II** analog protein (Map protein) from Staphylococcus **aureus**)

L6 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 29 May 2000
ACCESSION NUMBER: 2000:355305 HCAPLUS
DOCUMENT NUMBER: 134:16333
TITLE: Recombinant expression and neutralizing activity of an MHC class II binding epitope of **toxic shock** syndrome toxin-1
AUTHOR(S): Rubinchik, Evelina; Chow, Anthony W.
CORPORATE SOURCE: Division of Infectious Diseases, Department of Medicine, Canadian Bacterial Disease Network, University of British Columbia, Vancouver, BC, V5Z 3J5, Can.
SOURCE: Vaccine (2000), 18(21), 2312-2320
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Toxic shock** syndrome (**TSS**) is caused by the staphylococcal superantigen, TSST-1. The MHC class II binding domain of TSST-1 containing a conserved sequence with other related staphylococcal enterotoxins, comprising TSST-1 residues 47-64 [T(47-64)], was expressed as a fusion protein with either glutathione-S-transferase (GST47-64), filamentous phage coat protein (pIII47-64), or E. coli outer membrane porin protein (OprF47-64), or synthesized as a peptide conjugated to bovine serum albumin, BSA47-64. GST47-64, OprF47-64 and BSA47-64, but not pIII47-64, all induced high-titer T(47-64)-specific antibodies in Balb/c mice. However, only anti-GST47-64 antibodies inhibited 125I-TSST-1 binding to MHC class II and abrogated TSST-1-induced T cell mitogenesis and TNFα secretion in human peripheral blood mononuclear cells. Purified GST47-64 also inhibited 125I-TSST-1 binding in a dose-dependent manner. These findings suggest that GST47-64 may have potential as a recombinant peptide vaccine or TSST-1 receptor inhibitor against **TSS**.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 10 Dec 1999
ACCESSION NUMBER: 1999:782771 HCAPLUS

DOCUMENT NUMBER: 132:249862
TITLE: The effect of site-specific monoclonal antibodies directed to **toxic shock** syndrome toxin-1 in experimental Staphylococcus aureus arthritis
AUTHOR(S): Verdrengh, M.; Kum, W.; Chow, A.; Tarkowski, A.
CORPORATE SOURCE: Department of Rheumatology, University of Goteborg, Goteborg, S-41346, Swed.
SOURCE: Clinical and Experimental Immunology (1999), 118(2), 268-270
CODEN: CEXIAL; ISSN: 0009-9104
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Staphylococcus aureus produces a large number of potential virulence factors, among these the superantigen **toxic shock** syndrome toxin-1 (TSST-1). We have recently demonstrated that TSST-1 is involved in the pathogenesis of septic arthritis. Recent data show that the TSST-1 mol. is composed of two distinct domains, one proposed to interact with T cell receptor (TCR) and one with the MHC class II. The aim of this study was to assess if interaction between TSST-1-specific MoAbs directed to sites on the MHC and/or TCR Vβ affects the development of exptl. S. aureus-induced arthritis. For that purpose we used a panel of seven MoAbs, which were injected i.p. before and after inoculation with a TSST-1-producing S. aureus strain. Administration of antibodies did not affect the development of arthritis, suggesting inefficacy of such a procedure in neutralization of exotoxin-mediated disease manifestations.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 05 Jul 1997
ACCESSION NUMBER: 1997:419898 HCAPLUS
DOCUMENT NUMBER: 127:148130
TITLE: Selective binding of bacterial toxins to major histocompatibility complex class II-expressing cells is controlled by invariant chain and HLA-DM
AUTHOR(S): Lavoie, Pascal M.; Thibodeau, Jacques; Cloutier, Isabelle; Busch, Robert; Sekaly, Rafick-P.
CORPORATE SOURCE: Laboratoire d'Immunologie, Institu de Recherches Cliniques de Montreal 110 ave Des Pins Ouest, Montreal, QC, H2W 1R7, Can.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1997), 94(13), 6892-6897
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bacterial superantigens (SAgs) bind to major histocompatibility complex (MHC) class II mols. and activate T cells in a Vβ-restricted fashion. We recently identified subsets of

HLA-DR1 mols. that show selectivity for SAgs. Here, we extend these observations by showing that different cell lineages demonstrate distinct SAg-binding specificities although they all express HLA-DR1. Indeed, B cells bind staphylococcal enterotoxin A (SEA) and **toxic shock** syndrome toxin 1 (TSST-1) with high affinity while staphylococcal enterotoxin B (SEB) binding is barely detectable. In contrast, DR1-transfected HeLa cells show efficient binding of SEB, but not of SEA or TSST-1. We investigated the class II maturation events required for efficient interaction with SAgs and found that the ability of cells to bind and present the toxins can be drastically modulated by coexpression of the class II-associated invariant chain (Ii) and HLA-DM. SEA binding to DR1 mols. required coexpression of Ii, whereas TSST-1 binding was selectively enhanced by DM. Binding of SEB was affected by cell type-specific factors other than Ii or DM. The selectivity of SAgs for different MHC class II populations was minimally affected by HLA-DR intrinsic polymorphism and could not be explained by binding to alternative sites on DR mols. Our results indicate that SAgs are sensitive to structural heterogeneity in class II mols., which is consequent to the differential regulation of expression of antigen processing cofactors. Therefore, we speculate that Staphylococcus **aureus** have retained the ability to express numerous SAgs in adaptation to the microheterogeneity displayed by **MHC class II** mols. and that this may relate to their ability to infect different tissues.

L6 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 14 Apr 1997
ACCESSION NUMBER: 1997:242310 HCAPLUS
DOCUMENT NUMBER: 126:262913
TITLE: T-cell proliferation to superantigen-releasing Staphylococcus **aureus** by **MHC class II**-bearing keratinocytes under protection from bacterial cytolysin
AUTHOR(S): Tokura, Yoshiki; Furukawa, Fukumi; Wakita, Hisashi; Yagi, Hiroaki; Ushijima, Tsutomu; Takigawa, Masahiro
CORPORATE SOURCE: Department of Dermatology, Hamamatsu University School of Medicine, Hamamatsu, 431-31, Japan
SOURCE: Journal of Investigative Dermatology (1997), 108(4), 488-494
CODEN: JIDEAE; ISSN: 0022-202X
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Skin colonization with Staphylococcus aureus may exacerbate skin **disorders** by activation of lesional **T cells** with release of superantigens. Although T cells are effectively stimulated by staphylococcal superantigens in the presence of epidermal accessory cells, it remains to be elucidated whether in vivo cutaneous colonization with S. aureus can activate T cells. We examined how T cells are stimulated in the presence of keratinocytes by mitomycin C (MMC)-treated S. aureus that are unable to propagate but retain their ability to produce superantigens. Peripheral blood mononuclear cells (PBMCs) proliferated well in response to MMC-treated superantigen-producing S. aureus and

bacterial supernatants. When purified T cells were cultured with MMC-treated S. aureus or supernatant in the presence of interferon-γ-pre-treated keratinocytes, the supernatant, but not MMC-treated S. aureus, stimulated T cells. MMC-treated S. aureus had a cytotoxic effect on keratinocytes. Furthermore, keratinocytes were highly susceptible to α-toxin compared with monocytes and B cells functioning as accessory cells in PBMCs. This suggests that a lack of response of T cells to S. aureus plus keratinocytes is due to damage of superantigen-presenting function of keratinocytes by cytolysin. The activity of α-toxin was much less stable than that of superantigen during incubation. Given that S. aureus-colonized skin provides circumstances in which viable keratinocytes are exposed to superantigens but not to active cytolysin(s), skin-infiltrating T cells may be effectively stimulated by S. aureus.

L6 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 09 Apr 1997
ACCESSION NUMBER: 1997:228380 HCAPLUS
DOCUMENT NUMBER: 126:237341
TITLE: **Major histocompatibility complex class II** region confers susceptibility to Staphylococcus **aureus** arthritis
AUTHOR(S): Abdelnour, A.; Zhao, Yi-Xue; Holmdahl, R.; Tarkowski, A.
CORPORATE SOURCE: Departments of Rheumatology and Clinical Immunology, University of Goteborg, Goteborg, S-413 46, Swed.
SOURCE: Scandinavian Journal of Immunology (1997), 45(3), 301-307
CODEN: SJIMAX; ISSN: 0300-9475
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The importance of the **MHC class II** region for the development of septic arthritis was studied in a murine model of induced Staphylococcus **aureus** arthritis. In the first experiment **MHC class II** deficient mice (Aβ-/-) and their heterozygous (Aβ+/-) littermates were i.v. inoculated with a single dose of **toxic shock** syndrome toxin-1 producing S. **aureus** LS-1 strain. The expression of class II MHC mols. increases the prevalence and severity of arthritis. To analyze the impact of MHC class II haplotypes on the disease onset and progression the authors used congenic C3H.NB, C3H.Q and C3H/HeJ mice in the second set of expts. The results show that C3H/HeJ mice developed the highest frequency and the most severe course of arthritis compared with C3H.NB and C3H.Q animals. Immunohistochem. anal. of arthritic joints revealed equal number of macrophages, CD4+ and CD8+ lymphocytes in the inflamed synovia in all the congenic mice. In contrast, the number of MHC class II expressing cells was higher in the arthritic joints of C3H/HeJ mice compared with the congenic strains. Furthermore, serum levels of proarthritogenic cytokines, such as tumor necrosis factor and interleukin-6 were higher in C3H/HeJ group. This study indicates that **MHC class**

II expression is necessary for the development of S. **aureus** arthritis in mice and that different **MHC class II** haplotypes confer varying susceptibility for development of joint inflammation induced by staphylococci.

L6 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 26 Jul 1996
ACCESSION NUMBER: 1996:440902 HCAPLUS
DOCUMENT NUMBER: 125:84646
TITLE: Protective effects of mutated superantigens
INVENTOR(S): Marrack, Philippa; Kappler, John W.; Shimonkevitz, Richard; Matsumura, Masazumi
PATENT ASSIGNEE(S): National Jewish Center for Immunology and Respiratory Medicine, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9614744	A1	19960523	WO 1995-US14639	19951108
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9641065	A1	19960606	AU 1996-41065	19951108

PRIORITY APPLN. INFO.: US 1994-338373 A 19941114
WO 1995-US14639 W 19951108

AB The present invention includes a method for preventing and treating the toxic effects of a superantigen and for modifying **pathogenic T cell** responses in **disease**. Superantigen mols. are modified or mutated so that they no longer have the pathol. effects of a superantigen, but are capable of eliciting an antibody response which crossreacts with and protects against the native superantigen. The mols. are useful, for example, as a vaccine. Mutated or modified superantigens that continue to interact with specific TCR Vβ-expressing subsets of T cells are also used ot modify the target T cell population in a Vβ-specific manner. The mutated superantigen disclosed here is **toxic shock** syndrome toxin TSST-1 of Staphylococcus aureus.

L6 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 23 Mar 1996
ACCESSION NUMBER: 1996:171143 HCAPLUS
DOCUMENT NUMBER: 124:314959
TITLE: Difference in human and murine T cell responsiveness to staphylococcal enterotoxins is determined by activities of MHC class II-positive cells

AUTHOR(S): Nishikawa, Mizuho; Yagi, Junji; Yan, Xiao Jie; Oshimi, Yoko; Miyazaki, Shunichi; Uchiyama, Takehiko
CORPORATE SOURCE: Dep. Microbiol. Immunol., Tokyo Women's Med. Coll., Tokyo, 162, Japan
SOURCE: Tokyo Joshi Ika Daigaku Zasshi (1996), 66(1/2), 20-31
CODEN: TJIZAF; ISSN: 0040-9022
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bacterial superantigens (SAGs) bind to major histocompatibility complex (MHC) class II mols. on accessory cells (AC) and stimulate T cells upon interaction with the Vβ portion of the T cell receptor (TCR). We have recently shown that bacterial SAGs produced by Staphylococcus aureus, staphylococcal enterotoxin A (SEA), SEB, SEC, and **toxic shock** syndrome toxin-1 (TSST-1) can all stimulate human peripheral blood mononuclear cells (PBMC) at very minute doses of antigens (≥10-4 ng/mL). When murine peripheral lymphocytes are used, SEs and TSST-1 have been segregated into 2 groups according to potency. SEA and TSST-1 are equally strong stimulators of murine peripheral lymphocytes (≥10-4 ng/mL), whereas the responses of murine peripheral lymphocytes to SEB and SEC required 103-104-fold greater doses. However, it is still unclear whether this difference between the murine and human responses to SEB and SEC is due to a difference in T cell responsiveness or a difference in the activity of AC. In this study, the response of identical murine T cell prepns. to SEB showed a preference for human AC over murine AC. Thus, the results indicated that the difference in response to SEB is primarily due to a difference in the activity of AC. Furthermore, the Ca2+ concentration of murine T cells responding to SEB presented by human AC was higher than that of those responding to SEB presented by murine AC, indicating that different accessory activity influences T cell activation from the early phase of signal transduction.

L6 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 30 Aug 1995
ACCESSION NUMBER: 1995:766744 HCAPLUS
DOCUMENT NUMBER: 123:164792
TITLE: Crystal structure of the superantigen enterotoxin C2 from Staphylococcus aureus reveals a zinc-binding site
AUTHOR(S): Papageorgiou, Anastassios C.; Acharya, K. Ravi; Shapiro, Robert; Passalacqua, Edward F.; Brehm, Rossalyn D.; Tranter, Howard S.
CORPORATE SOURCE: School of Biology and Biochemistry, University of Bath, Bath, BA2 7AY, UK
SOURCE: Structure (London) (1995), 3(8), 769-79
CODEN: STRUE6; ISSN: 0969-2126
PUBLISHER: Current Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Staphylococcus **aureus** enterotoxin C2 (SEC2) belongs to a family of proteins, termed superantigens, that form complexes with **class II MHC** mols. enabling them to activate a substantial number of T cells. Although superantigens seem

to act by a common mechanism, they vary in many of their specific interactions and biol. properties. Comparison of the structure of SEC2 with those of two other superantigens - staphylococcal enterotoxin B (SEB) and **toxic shock** syndrome toxin-1 (TSST-1) - may provide insight into their mode of action. The crystal structure of SEC2 has been determined at 2.0 Å resolution The overall topol. of the mol. resembles that of SEB and TSST-1, and the regions corresponding to the MHC class II and T-cell receptor binding sites on SEB are quite similar in SEC2. A unique feature of SEC2 is the presence of a zinc ion located in a solvent-exposed region at the interface between the 2 domains of the mol. The zinc ion is coordinated to Asp83, His118, His122 and Asp9* (from the neighboring mol. in the crystal lattice). Atomic absorption spectrometry demonstrates that zinc is also bound to SEC2 in solution SEC2 appears to be capable of binding to MHC class II mols. in much the same manner as SEB. However, structure-function studies have suggested an alternative binding mode that involves a different site on the toxin. The zinc ion of SEC2 lies within this region and thus may be important for complex formation, for example by acting as a bridge between the two mols. Other possible roles for the metal cation, including a catalytic one, are also considered.

L6 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 02 Apr 1994
ACCESSION NUMBER: 1994:161078 HCAPLUS
DOCUMENT NUMBER: 120:161078
TITLE: Binding sites for bacterial and endogenous retroviral superantigens can be dissociated on major histocompatibility complex class II molecules
AUTHOR(S): Thibodeau, Jacques; Labrecque, Nathalie; Denis, Francois; Huber, Brigitte T.; Sekaly, Rafick Pierre
CORPORATE SOURCE: Lab. Immunol., Inst. Rech. Clin. Montreal, Montreal, QC, H2W 1R7, Can.
SOURCE: Journal of Experimental Medicine (1994), 179(3), 1029-34
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bacterial and retroviral superantigens (SAGs) interact with major histocompatibility complex (MHC) class II mols. and stimulate T cells upon binding to the Vβ portion of the T cell receptor. Whereas both types of mols. exert similar effects on T cells, they have very different primary structures. Amino acids critical for the binding of bacterial toxins to class II mols. have been identified but little is known of the mol. interactions between class II and retroviral SAGs. To determine whether both types of superantigens interact with the same regions of **MHC class II** mols., the authors have generated mutant HLA-DR mols. which have lost the capacity to bind three bacterial toxins (Staphylococcus **aureus** enterotoxin A [SEA], S. **aureus** enterotoxin B [SEB], and **toxic shock** syndrome toxin 1 [TSST-1]). Cells expressing these mutated class II mols. efficiently presented two retroviral SAGs (Mtv-9 and Mtv-7) to T cells while they were unable to present the

bacterial SAGs. These results demonstrate that the binding sites for both types of SAGs can be dissociated

L6 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 06 Apr 1991
ACCESSION NUMBER: 1991:119927 HCAPLUS
DOCUMENT NUMBER: 114:119927
TITLE: Mechanism of Staphylococcus aureus exotoxin A inhibition of Ig production by human B cells
AUTHOR(S): Moseley, Annemarie B.; Huston, David P.
CORPORATE SOURCE: Dep. Med., Baylor Coll. Med., Houston, TX, 77030, USA
SOURCE: Journal of Immunology (1991), 146(3), 826-32
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects were examined of Staphylococcus enterotoxin A (SEA) on proliferation and Ig production of highly purified human B cells. The binding of SEA to **MHC class II** mols.
on B cells does not alter their ability to proliferate in response to S. **aureus** Cowan strain I (SAC) or to produce Ig in response to SAC plus rIL-2. In contrast, the anti-DR mAb L243 inhibited both B cell proliferation and Ig production Unable to determine a direct effect of SEA on B cell function, it was investigated whether the capacity of SEA to inhibit SAC-induced Ig production by PBMC was T cell-dependent. The results demonstrated that in the presence of **T cells**, under appropriate **conditions**,
SEA can either function as a nominal antigen for stimulation of B cell proliferation and Ig production or induce T cell-mediated suppression of Ig production SEA-induced Ig production required T cell help, which was dependent on pretreatment of the T cells with irradiation or mitomycin C; Ig production was not induced by SEA in the absence of T cells or in the presence of untreated T cells. Furthermore, SEA inhibited Ig production in SAC-stimulated cultures of autologous B cells and untreated T cells; pretreatment of the T cells with irradiation or mitomycin C abrogated SEA-induced inhibition of Ig production Thus, T cell suppression of SAC-induced Ig production was dependent on T cell proliferation. Similar results were observed with both SEA and **toxic shock** syndrome toxin 1.

L6 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 13 Oct 1990
ACCESSION NUMBER: 1990:530280 HCAPLUS
DOCUMENT NUMBER: 113:130280
TITLE: The α1 domain of the HLA-DR molecule is essential for high-affinity binding of the **toxic shock** syndrome toxin-1
AUTHOR(S): Karp, David R.; Teletski, Christina L.; Scholl, Paul; Geha, Raif; Long, Eric O.
CORPORATE SOURCE: Lab. Immunogenet., Natl. Inst. Allergy and Infect. Dis., Bethesda, MD, 20892, USA
SOURCE: Nature (London, United Kingdom) (1990), 346(6283), 474-6
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several exoproteins from the bacterium Staphylococcus **aureus** are highly potent polyclonal activators of T cells in the presence of cells bearing **class II** antigens of the **major histocompatibility complex** (MHC). These toxins, including the **toxic shock** syndrome toxin (TSST-1), act a nanomolar concns., bind directly to class II mols., and do not require the processing typical of nominal antigen. Each toxin is capable of stimulating a subpopulation of peripheral T lymphocytes bearing particular Vβ sequences as part of their αβ T-cell receptors. It is not known how these so-called superantigens bind to class II and how this binding stimulates T cells. The different affinities of TSST-1 for human class II mols. DR and DP were exploited to define the region of a class II mol. necessary for high-affinity binding. Using chimeric α- and β-chains of DR and DP expressed at the surface of transfected murine fibroblasts and a binding assay with TSST-1, it was shown that the α1 domain of DR is essential for high-affinity binding, and further that TSST-1 binding did not prevent subsequent binding of a DR-restricted antigenic peptide. This is compatible with a model of superantigen making external contacts with both class II and T cells receptor, and suggests that the Vβ portion of the T-cell receptor interacts with the nonpolymorphic α-chain of DR.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER, PASCAL, DISSABS, FEDRIP' ENTERED AT 15:44:00 ON 30 APR 2004)

L7 105 SEA ABB=ON PLU=ON L6
L8 52 DUP REM L7 (53 DUPLICATES REMOVED)

L9 26 SEA ABB=ON PLU=ON L8 AND (THERAP? OR TREAT? OR PREVENT? OR MODULAT? OR SUPPRESS? OR INHIBIT?)

L9 ANSWER 1 OF 26 MEDLINE on STN
ACCESSION NUMBER: 2003199793 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12720278
TITLE: **Therapeutic** approaches to superantigen-based diseases: a review.
AUTHOR: Hong-Geller Elizabeth; Gupta Goutam
CORPORATE SOURCE: Los Alamos National Laboratory, Biosciences Division, HRL-1, MS-M888, Los Alamos, NM 87545, USA.
SOURCE: Journal of molecular recognition : JMR, (2003 Mar-Apr) 16 (2) 91-101. Ref: 86
Journal code: 9004580. ISSN: 0952-3499.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 20030430
Last Updated on STN: 20040115
Entered Medline: 20040114

AB Superantigens secreted by the bacterial pathogen Staphyloccocus **aureus** are extremely potent toxins that overstimulate the

host immune system by binding to the **MHC class II** and T cell receptors and activating a large population of T cells. Superantigen infection has been shown to be the causative agents in acute diseases, food poisoning and **toxic shock** syndrome, and in more chronic conditions such as inflammatory skin diseases. In addition to the toll on public health, S. aureus superantigens also represent a potential biothreat to our national security. To address these risks, a number of different **therapeutic** strategies have been developed that target different aspects of the pathogenic mechanism of S. aureus and superantigen infection. These **therapies,** which encompass strategies as diverse as production of neutralizing antibodies, **inhibitory** peptide/receptor design and blockage of superantigen gene transcription, are being tested for **treatment** of established S. aureus infections in pre- and post-exposure scenarios. In this review, we will describe these different strategies and their efficacies in **inhibition** of superantigen-induced effects in the host, and present the future outlook for successfully producing **therapies** for superantigen-based disease.

L9 ANSWER 2 OF 26 MEDLINE on STN
ACCESSION NUMBER: 2002640671 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12399195
TITLE: Epitope mapping of neutralizing TSST-1 specific antibodies induced by immunization with toxin or toxoids.
AUTHOR: Gampfer Jorg M; Samstag Aysen; Waclavicek Martina; Wolf Hermann M; Eibl Martha M; Gulle Heinz
CORPORATE SOURCE: Biomedizinische Forschungsgesellschaft mbH, Schwarzspanierstrasse 15/1/19, A-1090, Vienna, Austria.. joerg.gampfer@biomed-research.at
SOURCE: Vaccine, (2002 Nov 1) 20 (31-32) 3675-84. Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 20021026
Last Updated on STN: 20030531
Entered Medline: 20030530

AB **Toxic shock** syndrome toxin-1 (TSST-1), a superantigen produced by Staphylococcus aureus, is a potent stimulator of the immune system. T-cells are activated by crosslinking of MHC class II molecules on antigen presenting cells with T-cell receptors (TCR). TSST-1 is associated with the majority of the cases of menstrual staphylococcal **toxic shock,** a severe and life-threatening multisystem disorder. Even though antibody mediated protection has been studied, information on antibody specificity directed to individual antigenic determinants of the protein is incomplete.To obtain immunogens with low toxicity, we generated a double-site mutant (dmTSST-1), modified at solvent-exposed residues predicted to be important for both **MHC class II** and TCR binding, and

detoxified recombinantly expressed TSST-1 (rTSST-1) as well as native TSST-1 (nTSST-1) isolated from Staphylococcus **aureus** by **treatment** with formaldehyde. Rabbits were immunized with rTSST-1, nTSST-1, dmTSST-1, and formaldehyde inactivated toxoids. The sera obtained were used to map the antigen-reactive regions of the molecule and to identify specificities of antibodies induced by immunization with the different antigens. To detect linear antigenic epitopes of TSST-1 the reactivity of the sera with 11-meric peptides having an overhang of four residues, covering the entire molecule of TSST-1, have been studied. We found that sera of TSST-1 immunized rabbits predominantly reacted with N-terminal residues 1-15, while sera generated with formaldehyde inactivated toxoid recognized a total of 7 regions located at the N- and C-terminus and internal sites of TSST-1. Despite different specificities all sera were able to **inhibit** TSST-1 induced proliferation of human mononuclear cells.

L9 ANSWER 3 OF 26 MEDLINE on STN
ACCESSION NUMBER: 97338115 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9192662
TITLE: Selective binding of bacterial toxins to major histocompatibility complex class II-expressing cells is controlled by invariant chain and HLA-DM.
AUTHOR: Lavoie P M; Thibodeau J; Cloutier I; Busch R; Sekaly R P
CORPORATE SOURCE: Laboratoire d'Immunologie, Institut de Recherches Cliniques de Montreal 110 ave Des Pins Ouest, Montreal, PQ H2W 1R7, Canada.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1997 Jun 24) 94 (13) 6892-7.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970805
Last Updated on STN: 19970805
Entered Medline: 19970721

AB Bacterial superantigens (SAgs) bind to major histocompatibility complex (MHC) class II molecules and activate T cells in a Vbeta-restricted fashion. We recently identified subsets of HLA-DR1 molecules that show selectivity for SAgs. Here, we extend these observations by showing that different cell lineages demonstrate distinct SAg-binding specificities although they all express HLA-DR1. Indeed, B cells bind staphylococcal enterotoxin A (SEA) and **toxic shock** syndrome toxin 1 (TSST-1) with high affinity while staphylococcal enterotoxin B (SEB) binding is barely detectable. In contrast, DR1-transfected HeLa cells show efficient binding of SEB, but not of SEA or TSST-1. We investigated the class II maturation events required for efficient interaction with SAgs and found that the ability of cells to bind and present the toxins can be drastically **modulated** by coexpression of the class II-associated invariant chain (Ii) and HLA-DM. SEA binding to DR1 molecules required coexpression of Ii, whereas TSST-1

binding was selectively enhanced by DM. Binding of SEB was affected by cell type-specific factors other than Ii or DM. The selectivity of SAgs for different MHC class II populations was minimally affected by HLA-DR intrinsic polymorphism and could not be explained by binding to alternative sites on DR molecules. Our results indicate that SAgs are sensitive to structural heterogeneity in class II molecules, which is consequent to the differential regulation of expression of antigen processing cofactors. Therefore, we speculate that Staphylococcus **aureus** have retained the ability to express numerous SAgs in adaptation to the micro-heterogeneity displayed by **MHC class II** molecules and that this may relate to their ability to infect different tissues.

L9 ANSWER 4 OF 26 MEDLINE on STN
ACCESSION NUMBER: 97232204 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9077479
TITLE: T-cell proliferation to superantigen-releasing Staphylococcus **aureus** by **MHC class II**-bearing keratinocytes under protection from bacterial cytolysin.
AUTHOR: Tokura Y; Furukawa F; Wakita H; Yagi H; Ushijima T; Takigawa M
CORPORATE SOURCE: Department of Dermatology, Hamamatsu University School of Medicine, Japan.
SOURCE: Journal of investigative dermatology, (1997 Apr) 108 (4) 488-94.
Journal code: 0426720. ISSN: 0022-202X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970422
Last Updated on STN: 20000303
Entered Medline: 19970409

AB Skin colonization with Staphylococcus aureus may exacerbate skin **disorders** by activation of lesional **T cells** with release of superantigens. Although T cells are effectively stimulated by staphylococcal superantigens in the presence of epidermal accessory cells, it remains to be elucidated whether in vivo cutaneous colonization with S. aureus can activate T cells. We examined how T cells are stimulated in the presence of keratinocytes by mitomycin C (MMC)-**treated** S. aureus that are unable to propagate but retain their ability to produce superantigens. Peripheral blood mononuclear cells (PBMCs) proliferated well in response to MMC-**treated** superantigen-producing S. aureus and bacterial supernatants. When purified T cells were cultured with MMC-**treated** S. aureus or supernatant in the presence of interferon-gamma-pre-**treated** keratinocytes, the supernatant, but not MMC-**treated** S. aureus, stimulated T cells. MMC-**treated** S. aureus had a cytotoxic effect on keratinocytes. Furthermore, keratinocytes were highly susceptible to alpha-toxin compared with monocytes and B cells functioning as accessory cells in PBMCs. This suggests that a lack of response of T cells to S. aureus plus

keratinocytes is due to damage of superantigen-presenting function of keratinocytes by cytolysin. The activity of alpha-toxin was much less stable than that of superantigen during incubation. Given that S. aureus-colonized skin provides circumstances in which viable keratinocytes are exposed to superantigens but not to active cytolysin(s), skin-infiltrating T cells may be effectively stimulated by S. aureus.

L9 ANSWER 5 OF 26 MEDLINE on STN
ACCESSION NUMBER: 91108048 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1988499
TITLE: Mechanism of Staphylococcus aureus exotoxin A **inhibition** of Ig production by human B cells.
AUTHOR: Moseley A B; Huston D P
CORPORATE SOURCE: Department of Medicine, Baylor College of Medicine, Houston, TX.
CONTRACT NUMBER: AI21289 (NIAID)
AI24664 (NIAID)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (1991 Feb 1) 146 (3) 826-32.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199102
ENTRY DATE: Entered STN: 19910329
Last Updated on STN: 19910329
Entered Medline: 19910225

AB Staphylococcus enterotoxins and **toxic shock** syndrome toxin 1 are members of a family of exoproteins that are produced by staphylococci and bind specifically to MHC class II molecules. Upon binding to MHC class II molecules, these exoproteins are potent stimulators of T cell proliferation via interaction with specific TCR V-beta segments of both CD4+ and CD8+ T cells. These exoproteins also directly stimulate monocytes to secrete IL-1 and TNF-alpha. Furthermore, these exoproteins have a profound **inhibitory** effect on Ig production by PBMC. We examined the effects of Staphylococcus enterotoxin A (SEA) on proliferation and Ig production of highly purified human B cells. Our results demonstrated that the binding of SEA to **MHC class II** molecules on B cells does not alter their ability to proliferate in response to Staphylococcus **aureus** Cowan strain I (SAC) or to produce Ig in response to SAC plus rIL-2. In contrast, the anti-DR mAb L243 **inhibited** both B cell proliferation and Ig production. Unable to determine a direct effect of SEA on B cell function, we investigated whether the capacity of SEA to **inhibit** SAC-induced Ig production by PBMC was T cell-dependent. Our results demonstrated that in the presence of **T cells**, under appropriate **conditions**, SEA can either function as a nominal Ag for stimulation of B cell proliferation and Ig production or induce T cell-mediated **suppression** of Ig production. SEA-induced Ig production required T cell help, which was dependent on pretreatment of the T cells with irradiation or mitomycin C; Ig production was not induced by SEA in the absence of T cells or in

the presence of untreated T cells. Furthermore, SEA **inhibited** Ig production in SAC-stimulated cultures of autologous B cells and untreated T cells; pretreatment of the T cells with irradiation or mitomycin C abrogated SEA-induced **inhibition** of Ig production. Thus, T cell **suppression** of SAC-induced Ig production was dependent on T cell proliferation. Similar results were observed with both SEA and **toxic shock** syndrome toxin 1.

L9 ANSWER 6 OF 26 MEDLINE on STN
ACCESSION NUMBER: 90332007 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2377209
TITLE: The alpha 1 domain of the HLA-DR molecule is essential for high-affinity binding of the **toxic shock** syndrome toxin-1.
AUTHOR: Karp D R; Teletski C L; Scholl P; Geha R; Long E O
CORPORATE SOURCE: Laboratory of Immunogenetics, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892.
SOURCE: Nature, (1990 Aug 2) 346 (6283) 474-6.
Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199009
ENTRY DATE: Entered STN: 19901012
Last Updated on STN: 19980206
Entered Medline: 19900906

AB Several exoproteins from the bacterium Staphylococcus **aureus** are highly potent polyclonal activators of T cells in the presence of cells bearing **class II** antigens of the **major histocompatibility complex** (MHC). These toxins, including the **toxic shock** syndrome toxin (TSST-1), act at nanomolar concentrations, bind directly to class II molecules, and do not require the processing typical of nominal antigen. Each toxin is capable of stimulating a subpopulation of peripheral T lymphocytes bearing particular V beta sequences as part of their alpha beta T-cell receptors. It is not known how these so-called 'superantigens' bind to class II and how this binding stimulates T cells. In this study, the different affinities of TSST-1 for human class II molecules DR and DP were exploited to define the region of a class II molecule necessary for high-affinity binding. Using chimaeric alpha- and beta-chains of DR and DP expressed at the surface of transfected murine fibroblasts and a binding assay with TSST-1, it was shown that the alpha 1 domain of DR is essential for high-affinity binding, and further that TSST-1 binding did not **prevent** subsequent binding of a DR-restricted antigenic peptide. This is compatible with a model of superantigen making external contacts with both class II and T cell receptor, and suggests that the V beta portion of the T-cell receptor interacts with the nonpolymorphic alpha-chain of DR.

L9 ANSWER 7 OF 26 EMBASE on STN
ACCESSION NUMBER: 2004079921 EMBASE

TITLE: Design of chimeric receptor mimics with different TcRVβ isoforms: Type-specific **inhibition** of superantigen pathogenesis.
AUTHOR: Hong-Geller E.; Mollhoff M.; Shiflett P.R.; Gupta G.
CORPORATE SOURCE: G. Gupta, Los Alamos National Laboratory, Biosciences Division, HRL-1, Los Alamos, NM 87544, United States. gxg@lanl.gov
SOURCE: Journal of Biological Chemistry, (13 Feb 2004) 279/7 (5676-5684).
Refs: 39
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The Staphylococcus **aureus** enterotoxins (S.E.) A-I, and **toxic-shock** syndrome toxin TSST-1 act as superantigens to cause overstimulation of the host immune system, leading to the onset of various diseases including food poisoning and **toxic shock** syndrome. SAgs bind as intact proteins to the DRα1 domain of the **MHC class II** receptor and the TcRVβ domain from the T cell receptor and cause excessive release of cytokines such as IL-2, TNF-α, and IFN-γ, and hyperproliferation of T cells. In addition, different SAgs bind and activate different TcRVβ isoforms during pathogenesis of human immune cells. These two properties of SAgs prompted us to design several chimeric DRα1-linker-TcRVβ proteins using different TcRVβ isoforms to create chimeras that would specifically **inhibit** the pathogenesis of SAgs against which they were designed. In this study, we compare the design, interaction, and **inhibitory** properties of three different DRα1-linker-TcRVβ chimeras targeted against three different SAgs, SEB, SEC3, and TSST-1. The **inhibitory** properties of the chimeras were tested by monitoring IL-2 release and T cell proliferation using a primary human cell model. We demonstrate that the three chimeras specifically **inhibit** the pathogenesis of their target superantigen. We performed molecular modeling to analyze the structural basis of the type specificity exhibited by different chimeras designed against their target SAgs, examine the role of the linker in determining binding and specificity, and suggest site-specific mutations in the chimera to enhance binding affinity. The fact that our strategy works equally well for SEB and TSST-1, two widely different phylogenic variants, suggests that the DRα1-linker-TcRVβ chimeras may be developed as a general **therapy** against a broad spectrum of superantigens released during Staphylococcal infection.

L9 ANSWER 8 OF 26 EMBASE on STN
ACCESSION NUMBER: 2002432880 EMBASE
TITLE: The Staphylococcus aureus Map protein is an immunomodulator that interferes with T cell-mediated responses.
AUTHOR: Lee L.Y.; Miyamoto Y.J.; McIntyre B.W.; Hook M.;

McCrea K.W.; McDevitt D.; Brown E.L.
CORPORATE SOURCE: E.L. Brown, Ctr. for Extracellular Matrix Biol., TX A/M Univ. Syst. Hlth. Sci. Ctr., A. B. Alkek Inst. Biosci./Technol., 2121 West Holcombe Boulevard, Houston, TX 77030-7552, United States. ebrown@ibt.tamu.edu
SOURCE: Journal of Clinical Investigation, (2002) 110/10 (1461-1471).
Refs: 70
ISSN: 0021-9738 CODEN: JCINAO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Staphylococcus **aureus** (SA) is an opportunistic pathogen that affects a variety of organ systems and is responsible for many diseases worldwide. SA express an **MHC class II** analog protein (Map), which may potentiate SA survival by **modulating** host immunity. We tested this hypothesis in mice by generating Map-deficient SA (Map-SA) and comparing disease outcome to wild-type Map(+)SA-infected mice. Map(-)SA-infected mice presented with significantly reduced levels of arthritis, osteomyelitis, and abscess formation compared with control animals. Furthermore, Map(-)SA-infected nude mice developed arthritis and osteomyelitis to a severity similar to Map(+)SA-infected controls, suggesting that **T cells** can affect **disease** outcome following SA infection and Map may attenuate cellular immunity against SA. The capacity of Map to alter T cell function was tested more specifically in vitro and in vivo using native and recombinant forms of Map. T cells or mice **treated** with recombinant Map had reduced T cell proliferative responses and a significantly reduced delayed-type hypersensitivity response to challenge antigen, respectively. These data suggest a role for Map as an immunomodulatory protein that may play a role in persistent SA infections by affecting protective cellular immunity.

L9 ANSWER 9 OF 26 EMBASE on STN
ACCESSION NUMBER: 2001371293 EMBASE
TITLE: **Toxic shock** syndrome and bacterial superantigens: An update.
AUTHOR: McCormick J.K.; Yarwood J.M.; Schlievert P.M.
CORPORATE SOURCE: J.K. McCormick, Department of Microbiology, Univ. of Minnesota Medical School, Minneapolis, MN 55455, United States. jmccormi@lenti.med.umn.edu
SOURCE: Annual Review of Microbiology, (2001) 55/- (77-104).
Refs: 180
ISSN: 0066-4227 CODEN: ARMIAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English

SUMMARY LANGUAGE: English

AB **Toxic shock** syndrome (**TSS**) is an acute onset illness characterized by fever, rash formation, and hypotension that can lead to multiple organ failure and lethal shock, as well as desquamation in patients that recover. The disease is caused by bacterial superantigens (SAGs) secreted from Staphylococcus **aureus** and group A streptococci. SAGs bypass normal antigen presentation by binding to **class II major histocompatibility complex** molecules on antigen-presenting cells and to specific variable regions on the β-chain of the T-cell antigen receptor. Through this interaction, SAGs activate T cells at orders of magnitude above antigen-specific activation, resulting in massive cytokine release that is believed to be responsible for the most severe features of **TSS**. This review focuses on clinical and epidemiological aspects of **TSS**, as well as important developments in the genetics, biochemistry, immunology, and structural biology of SAGs. From the evolutionary relationships between these important toxins, we propose that there are five distinct groups of SAGs.

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ACCESSION NUMBER: 2001371198 EMBASE

TITLE: Use of intravenous immunoglobulin in the **treatment** of staphylococcal and streptococcal **toxic shock** syndromes and related illnesses.

AUTHOR: Schlievert P.M.

CORPORATE SOURCE: Dr. P.M. Schlievert, Department of Microbiology, Univ. of Minnesota Medical School, 420 Delaware St SE, Minneapolis, MN 55455, United States

SOURCE: Journal of Allergy and Clinical Immunology, (2001) 108/4 SUPPL. (S107-S110).
Refs: 12
ISSN: 0091-6749 CODEN: JACIBY

COUNTRY: United States

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Pyrogenic toxin superantigens comprise a large family of exotoxins made by Staphylococcus **aureus** and group A streptococci. These toxins include **toxic shock** syndrome toxin-1, the staphylococcal enterotoxins, and the streptococcal pyrogenic exotoxins (synonyms: scarlet fever toxins and erythrogenic toxins), all of which have the ability to cause **toxic shock** syndromes and related illnesses. These toxins have a similar three-dimensional structure that allows them to interact with relatively invariant regions of **major histocompatibility complex class II** molecules on the surface of antigen-presenting cells and with certain variable regions of the T-cell receptor-β chain. The consequence of these interactions (and other immunobiological

properties of the toxins) is the exaggerated release of bioactive cytokines. The latter molecules are responsible for the clinical signs of illness associated with these toxins.

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ACCESSION NUMBER: 2001089054 EMBASE
TITLE: Role of superantigens in dermatology.
AUTHOR: De la Brassinne M.; Dezfoulian B.
CORPORATE SOURCE: Prof. M. De la Brassinne, Department of Dermatology, University of Liege, CHU Sart-Tilman - B 35, B - 4000 Sart Tilman Liege 1, Belgium
SOURCE: Advances in Experimental Medicine and Biology, (1999) 455/- (245-248).
Refs: 12
ISSN: 0065-2598 CODEN: AEMBAP
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
013 Dermatology and Venereology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Superantigens are very potent agonists of T-lymphocytes. The superantigenic types of reactions on various subsets of T-lymphocytes are compared with those of classical antigens and aspecific mitogens. The role they could play in skin disease is reviewed with special emphasis to acute and chronic diseases, auto-immunity, immediate type reactions, immunodeficiency, carcinogenesis, psoriasis and other inflammatory cutaneous conditions. The term "superantigen" has been used for the first time in 1989 by the group of Kappler and Marrack [1,2]. Superantigens are proteins produced by bacteria (mainly streptococci and staphylococci), by mycoplasma, by retroviruses and probably by numerous other viral, bacterial and parasitic micro-organisms. They interfere with the immune system by binding with **class II** proteins of the **major histocompatibility complex** (HLA-MHC) present on the antigen presenting cells (APC) on one side and with the variable part of the β-chain (Vβ) of the T cell receptor (TCR) on the other side. This binding of superantigen is like a "short circuit" between the two cells resulting in a massive, rapid and exponential proliferation of T-lymphocytes usually followed by death of most stimulated T cells. Moreover, an anergy is usually observed against further stimulations of surviving T cells. However, such an anergy is not specific of superantigenic response and can also be seen for classical nominal antigens, auto-antigens and even for nonspecific mitogens (PWM, PHA, Con A, pertussis toxin). The main characteristic of superantigens as compared to classical antigens is that they do not need maturation processing into antigenic peptides by the proteases in the APC. They are not presented in the groove made by **MHC class II** on APC and by TCR on T cells but outside this groove on the Vβ lateral side. The proportion of T-lymphocytes responding to a nominal antigen is about 1/1000 while the proportion of T-lymphocytes responding to a superantigen reaches 5 to 25 %. As compared to nonspecific mitogens

activating all T cells, superantigens display a specificity leading to the proliferation of subsets of T-lymphocytes via Vβ chain with a possible contribution of Vα chain and a very minor contribution of Dβ, Jβ and/or Jα. Depending on the subset of stimulated T cells and on the types of cytokines produced, the symptomatology and the syndromes induced are numerous and display a very wide range [3, 4, 5]. According to the stimulated subsets of T cells, different reactions can be observed: 1. CD 4(+) T helper: sudden immune reaction (for example: **toxic shock** syndrome). 2. T helper with secondary stimulation of B-lymphocytes: uncontrolled production of immunoglobulins (for example: staphylococcal scalded skin syndrome). 3. CD 8(+) T **suppresser**: immunosuppressor (for example: AIDS). 4. NK cells: carcinogenesis (for example: mammary tumor in mice) [6]. After intense stimulation, a large proliferation can be followed by a desequilibrium between subsets of T lymphocytes due to cell death and apoptosis leading to a secondary immunodepression and a down regulation of Ig mediated and delayed type hypersensitivities. Moreover, the surviving subsets of T cells are unable to react to further stimulation by other superantigens and also by classical antigens. This mechanism is responsible of a true anergy which is a peripheral tolerance phenomenon [7, 8]. Most of well known superantigens are of exogenous origin; they are produced by bacteria or viruses. Bacterial superantigens are mainly: 1) Staphyloccus **aureus: toxic shock** syndrome toxin (TSST1), staphylococcal enterotoxins (SE), exfoliative toxins (ExFT), 2) Streptococcal pyogenic enterotoxins (SPE), 3) Mycoplasma arthritidis mitogen (MAM), 4) Yersinia enterocolica antigen (YEA) and 5) Pseudomonas aeruginosa exotoxin (PE). Viral exogenous superantigens are known for murine leukaemia virus (MuLV), for human immunodeficiency virus (HIV) and for rabies. Molecules produced by viruses could enhance incorporation of the viral genome into the lost cells, increase T cell death and induce immunosuppression by activation of CD 8(+) T cells. In addition to these infectious agents producing characteristic identified superantigens, many other micro-organisms are most probably able to synthesize molecules with a superantigenic potential. A documentation is already available for toxoplasma gondii and candida albicans [9, 10]. Endogenous superantigens have been identified in mice. The minor antigen of immune stimulation (AgMIS) is coded by an endogenous provirus. The murine mammary tumor virus (MMTV) is transmitted by mendelian heredity and probably by breast feeding. Its expression at birth leads to a negative selection of reactive T-lymphocytes. In adults, it induces a stimulation of subsets of T cells followed by relative anergy. Its integration near a proto-oncongen is responsible for the mammary tumor [6, 10, 11]. It could play a partial role in auto-immune reaction induction through the production of IgG by activated B-lymphocytes or by reaction between TCR present on active T-lymphocytes and auto-antigens present in their peripheral homing location [6, 12]. The equivalent of MMTV has not yet been found in man but superantigenic mechanisms could well be involved in viral induced carcinogenesis, in auto-immune diseases and in congenital immunodeficiency. In dermatology, **diseases** and syndromes with superantigenic **pathogenicity** are most probably very numerous. Apart from well-defined superantigen diseases, many inflammatory skin disorders are associated with bacterial parasitic

colonies that could secrete superantigens. Superantigens actions are probably involved, at least in part, in the etiology or at least in some of the **pathogenic** mechanisms of such **disorders** [4, 6, 10]. We present in the list below several dermatological **conditions** with possible superantigenic **pathogenicity**: 1. Acute skin **diseases** caused by bacterial superantigenic toxins or by viral superantigens: infectious toxic dermatitis in menstrual and non menstrual **toxic shock** syndrome, toxic dermatitis in pseudo-**toxic shock** syndrome induced by Yersinia or pseudomonas, staphylococcal scalded skin syndrome, scarlet fever, erysipelas, cellulitis, fasciitis, purpura in septicemia, cutaneous symptoms of endocarditis, rabies. 2. Auto-immune chronic skin diseases: erythema marginatium in rheumatic fever, skin lesions of rheumatoid polyarthritis, Kawasaki's syndrome, lupus-like syndrome (lichenoid chronic graft versus host disease, mycoplasma arthritidis arthritis, lichen planus, acroscleroderma, mixed connective tissue disease). 3. Modifications of dermatoses induced by hypersensitivity reactions: **inhibition** of IgE mediated hypersensitivity through the skin in contact urticaria; flare-up after staphylococcal infection in atopic dermatitis; eczema vaccinatum, eczema herpeticum, Kaposi-Juliusberg's syndromes in atopic dermatitis: down regulation of delayed type hypersensitivity in contact dermatitis with **inhibition** of reaction to of patch tests. 4. Various vasculitis with dermatological symptoms during infections with special attention to sudden IgA mediated necrotizing vasculitis following infection by streptococci, staphylococci, clostridium perfringens and pseudomonas aeruginosa. 5. Neoplasic **disorders** in the **pathogenicity** of which viruses could act as superantigens beeing expressed near proto-oncogens. A documentation is already available for Kaposi's sarcoma (classical Mediterranean, endemic African and HIV associated), Burkitt's tumor, cutaneous T cell lymphoma (CTCL) such as Worringer Kolopp's disease (pagetoid reticulosis), mycosis fungoides, Sezary's syndrome and probably several forms of leukaemias. 6. Genetically pre-existing diseases in which superantigens can induce the onset, aggravate and induce relapses.

L9 ANSWER 12 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1998247944 EMBASE
TITLE: Roxithromycin down-**modulates** antigen-presenting and interleukin-1β- producing abilities of murine Langerhans cells.
AUTHOR: Ohshima A.; Tokura Y.; Wakita H.; Furukawa F.; Takigawa M.
CORPORATE SOURCE: A. Ohshima, Department of Dermatology, Hamamatsu Univ. School of Medicine, 3600 Handa-cho, Hamamatsu 431-3192, Japan
SOURCE: Journal of Dermatological Science, (1998) 17/3 (214-222).
Refs: 41
ISSN: 0923-1811 CODEN: JDSCEI
PUBLISHER IDENT.: S 0923-1811(98)00017-6
COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 013 Dermatology and Venereology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The immunomodulatory effect of the macrolide antibiotic, roxithromycin (RXM) on Langerhans cells (LC) was studied in mice. RXM **inhibited** the ability of LC to present superantigen and hapten to T cells at 100 μM. The superantigen-presenting activity of LC was more profoundly abrogated by RXM than the hapten-presenting activity. This functional reduction was partly attributed to an RXM-induced decrease in promotion of the expression of **major histocompatibility complex class II** molecules on LC. On the other hand, RXM down-**modulated** the production of interleukin-1β by LC at a lower concentration of 10 μM than concentrations that **inhibited** antigen presentation. These results imply that RXM exerts **therapeutic** effectiveness via not only bacteriocidal action but also **inhibitory** effect on the LC ability in **T-cell**-mediated cutaneous **diseases** that can be exacerbated by skin-colonized Staphylococcus **aureus**.

L9 ANSWER 13 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 96007555 EMBASE
DOCUMENT NUMBER: 1996007555
TITLE: Upregulation of IgE synthesis by staphylococcal **toxic shock** syndrome toxin-1 in peripheral blood mononuclear cells from patients with atopic dermatitis.
AUTHOR: Hofer M.F.; Lester M.R.; Schlievert P.M.; Leung D.Y.M.
CORPORATE SOURCE: Department of Paediatrics, National Jewish Ctr. for Immunology, 1400 Jackson Street,Denver, CO 80206, United States
SOURCE: Clinical and Experimental Allergy, (1995) 25/12 (1218-1227).
ISSN: 0954-7894 CODEN: CLEAEN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
013 Dermatology and Venereology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background. Atopic dermatitis (AD)is a chronic skin disease associated with increased IgE synthesis and colonization with Staphylococcus **aureus** secreting exotoxins, such as **Toxic Shock** Syndrome Toxin-1 (TSST-1). Objectives. In this study, we were interested in determining the in vitro effects of TSST-1 on IgE synthesis in peripheral blood mononuclear cells from patients with AD. Methods We stimulated peripheral blood mononuclear cells (PBMC) from AD patients with a wide range of TSST-1 concentrations and measured IgE synthesis by enzyme-linked immunosorbent assay (ELISA) after 14 days. Results. We show herein

that TSST-1 produced antagonistic effects on IgE synthesis by PBMC from AD patients, depending on the concentration used: IgE synthesis was **inhibited** at 1000 pg/mL ($P < 0.05$) and enhanced at 0.01 pg/mL ($P < 0.01$) of toxin. TSST-1 was found to induce the production of much higher amounts of interferon-gamma (IFNγ) at 1000 pg/mL than at 0.01 pg/mL of toxin ($P = 0.0001$). More importantly, immunoglobulin E (IgE) synthesis was enhanced by TSST-1 at 1 pg/mL In the presence of antibodies blocking IFNγ activity. The other immunoglobulin (Ig) isotypes were also increased after TSST-1 stimulation suggesting that the enhanced IgE synthesis was secondary to a polyclonal B cell activation rather than an isotype switch. TSST-1-stimulated IgE synthesis was T cell-dependent because purified tonsil B cells were only able to synthesize increased amounts of IgE when small numbers of T cells were added to the cultures. Anti-HLA-DR and anti-LFA-1 monoclonal antibodies (MoAb) **inhibited** TSST-1-enhanced IgE synthesis, suggesting that the bridging of the T cell receptor (TCR) and **major histocompatibility complex** (MHC) **class II** on B cells was necessary for activation of B cell differentiation. Conclusion. These data indicate that staphylococcal superantigens are able, at concentrations inducing low amounts of IFNγ, to stimulate IgE synthesis by PBMC from AD patients, and suggest that staphylococcal toxins may contribute to elevated IgE synthesis in AD.

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ACCESSION NUMBER: 95021430 EMBASE
DOCUMENT NUMBER: 1995021430
TITLE: Major histocompatibility complex class II binding site for streptococcal pyrogenic (erythrogenic) toxin A.
AUTHOR: Hartwig U.F.; Gerlach D.; Fleischer B.
CORPORATE SOURCE: Bernhard-Nocht Inst Tropic Medicine, Bernhard-Nocht-Street 74,D-20359 Hamburg, Germany
SOURCE: Medical Microbiology and Immunology, (1994) 183/5 (257-264).
ISSN: 0300-8584 CODEN: MMIYAO
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Streptococcal pyrogenic exotoxin A (SPEA) is an important pathogenicity factor of group A streptococci. It is a member of the family of 'superantigens' produced by Staphylococcus **aureus** and Streptococcus pyogenes and its T lymphocyte stimulating activity is involved into the pathogenesis of certain diseases caused by pyogenic streptococci. In this study we have produced and characterized recombinant SPEA molecules in Escherichia coli. These molecules are indistinguishable from natural SPEA in both T cell stimulatory and HLA class II binding activities. Human class II molecules are more efficient than mouse class II molecules in presenting SPEA to T cells. In binding tests to **major**

histocompatibility complex class **II**-positive cells SPEA competes with staphylococcal enterotoxin B and A but not with **toxic shock** syndrome toxin-1.

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ACCESSION NUMBER: 94124670 EMBASE
DOCUMENT NUMBER: 1994124670
TITLE: Cell adhesion molecules are co-receptors for staphylococcal enterotoxin B- induced T-cell activation and cytokine production.
AUTHOR: Krakauer T.
CORPORATE SOURCE: Applied Research Division, Bldg. 1425, USAMRIID,Frederick, MD 21702-5011, United States
SOURCE: Immunology Letters, (1994) 39/2 (121-125). ISSN: 0165-2478 CODEN: IMLED6
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Enterotoxins produced by Staphylococcus **aureus** are potent mitogens for human T cells and cause lethal **toxic shock**. These superantigens bind to **major histocompatibility complex class** **II** on antigen-presenting cells outside the conventional peptide-binding groove and stimulate T cells expressing certain T-cell receptor Vβ gene products. We investigated other cell-surface molecules on human peripheral blood mononuclear cells that can mediate staphylococcal enterotoxin B (SEB)-induced T-cell proliferation and cytokine production. SEB-induced proliferation of T cells was **inhibited** by monoclonal antibodies to CD2, CD11a, CD18, CD28, CD44, CD58 and ICAM-1. Anti-ICAM-1 also blocked the production of pro-inflammatory mediators, TNFα and IFNγ by SEB- stimulated T cells. These data suggest that the surface molecules, CD11a:CD18/ICAM-1, CD2/CD58, CD28 and CD44, are all important co-receptors for T-cell activation by superantigens. Thus, like conventional antigens, multiple stimulatory signals from the interactions of these receptors are required for superantigen-induced immune responses. Reducing toxic mediators such as TNFα and IFNγ by anti-ICAM antibodies in SEB-induced T-cell responses may be a useful **therapeutic** strategy to circumvent SEB toxicity and pathogenesis.

L9 ANSWER 16 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 90010425 EMBASE
DOCUMENT NUMBER: 1990010425
TITLE: The staphylococcal **toxic shock** syndrome toxin 1 triggers b cell proliferation and differentiation via major histocompatibility complex-unrestricted cognate T/B cell interaction.
AUTHOR: Mourad W.; Scholl P.; Diaz A.; Geha R.; Chatila T.
CORPORATE SOURCE: Division of Immunology, Children's Hospital, 300

Longwood Avenue,Boston, MA 02115, United States
SOURCE: Journal of Experimental Medicine, (1989) 170/6 (2011-2022).
ISSN: 0022-1007 CODEN: JEMEAV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The Staphylococcus **aureus** exotoxin **toxic shock** syndrome toxin 1 (TSST-1) is a potent activator of T cells and monocytes. We have recently demonstrated that TSST-1 is a superantigen that binds monomorphic determinants on **MHC class II** molecules. In the present study, we have examined the effects of TSST-1 on the activation and differentiation of high density human tonsillar B cells. TSST-1 bound to tonsillar B cells with high affinity and saturation kinetics. This binding was effectively **inhibited** by a combination of anti-HLA-DR and anti-HLA-DQ mAbs. **Treatment** of purified B cells with TSST-1 failed to induce B cell proliferation or Ig production. However, in the presence of irradiated T cells, TSST-1 induced resting B cells to proliferate and differentiate into Ig secretory cells. TSST-1 mimicked nominal antigen in that its induction of B cell responses was strictly dependent on physical contact between T and B cells, and was profoundly **inhibited** by anti-**MHC class II** mAbs, nti-CD3 mAbs, and, to a lesser extent, by anti-CD18 mAbs. However, unlike nominal antigen, TSST-1-mediated T/B cell interactions were MHC unrestricted. These results suggest that TSST-1 induces T cell-dependent B cell proliferation and differentiation by virtue of its ability to mediate MHC-unrestricted cognate T/B cell interaction via the TCR/CD3 complex and **MHC class II** antigens.

L9 ANSWER 17 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 89154806 EMBASE
DOCUMENT NUMBER: 1989154806
TITLE: **Toxic shock** syndrome toxin 1 binds to major histocompatibility complex class II molecules.
AUTHOR: Scholl P.; Diez A.; Mourad W.; Parsonnet J.; Geha R.S.; Chatila T.
CORPORATE SOURCE: Division of Allergy and Immunology, Children's Hospital, Boston, MA, United States
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1989) 86/11 (4210-4214).
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 025 Hematology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Toxic shock** syndrome toxin 1 (TSWST-1) is a 22-kDa exotoxin produced by strains of Staphylococcus **aureus** and implicated in the pathogenesis of **toxic shock** syndrome. In common with other staphylococcal exotoxins, TSST-1 has diverse immunological effects. These include the induction of interleukin 2 receptor expression, interleukin 2 synthesis, proliferation of human T lymphocytes, and stimulation of interleukin 1 synthesis by human monocytes. In the present study, we demonstrate that TSST-1 binds with saturation kinetics and with a dissociation constant of 17-43 nM to a single class of binding sites on human mononuclear cells. There was a strong correlation between the number of TSST-1 binding sites and the expression of **major histocompatibility complex class II** molecules, and interferon-γ induced the expression of class II molecules as well as TSST-1 binding sites on human skin-derived fibroblasts. Monoclonal antibodies to HLA-DR, but not to HLA-DP or HLA-DQ, strongly **inhibited** TSST-1 binding. Affinity chromatography of 125I-labeled cell membranes over TSST-1-agarose resulted in the recovery of two bands of 35 kDa and 31 kDa that comigrated, respectively, with the α and β chains of HLA-DR and that could be immunoprecipitated with anti-HLA-DR monoclonal antibodies. Binding of TSST-1 was demonstrated to HLA-DR and HLA-DQ L-cell transfectants. These results indicate that **major histocompatibility complex class II** molecules represent the major binding site for TSST-1 on human cells.

L9 ANSWER 18 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 84228551 EMBASE
DOCUMENT NUMBER: 1984228551
TITLE: Analysis of the mitogenic effects of **toxic shock** toxin on human peripheral blood mononuclear cells in vitro.
AUTHOR: Calvano S.E.; Quimby F.W.; Antonacci A.C.; et al.
CORPORATE SOURCE: Department of Surgery, Cornell University Medical College, New York, NY 10021, United States
SOURCE: Clinical Immunology and Immunopathology, (1984) 33/1 (99-110).
CODEN: CLIIAT
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 026 Immunology, Serology and Transplantation
004 Microbiology
052 Toxicology
LANGUAGE: English

AB It has been shown previously that the staphylococcal enterotoxins A and B are T-cell mitogens and also cause **inhibition** of murine plaque-forming cells generated in vitro. Similarly, **toxic shock** toxin, a 24,000-MW protein produced by **toxic shock**-associated strains of Staphylococcus **aureus**, is mitogenic and **inhibits** the generation of both murine and rabbit plaque-forming cells. In this study, an analysis of the T-cell response to **toxic shock** toxin over a broad dosage range (1 ng/ml to 5 μg/ml) with maximum proliferation at day 4 (96 hr) of culture. Heat **treatment**

(100°C for 60 min) of **toxic shock** toxin attenuated its mitogenic effects by only a small amount, and this attenuation could be reversed with increasing concentration of the toxin. By cytofluorography, both untreated and **toxic shock** toxin-**treated** small lymphocytes manifested normal percentages of OKT3+, OKT11+, OKT4+, OKT8+, HLA/DR+, and Leu-7+ cells. However, **toxic shock** toxin-induced blasts were 99% OKT11+ and expressed the receptor for interleukin 2 (89%-100% TAC+). Approximately 85% of the blasts were OKT4+, and 25% of the blasts were OKT8+. Proliferation of purified, double-rosetted T cells was enhanced monotonically by the addition of irradiated 'non-T' cells. Irradiated, monocyte-enriched non-T cells were 2.5 times more potent than unfractionated non-T cells in producing quantitatively similar proliferation by **toxic shock** toxin-stimulated, autologous T cells. In addition, preincubation of non-T cells for 24 hr with **toxic shock** toxin, followed by extensive washing and irradiation, induced substantial proliferation by unexposed, autologous T cells. These data show that **toxic shock** toxin is mitogenic for T cells and requires accessory cells for maximal activity. Further, this substance appears to induce both a subset of OKT4+ (**Class II MHC**-restricted) and OKT8+ (Class I MHC-restricted) blasts.

L9 ANSWER 19 OF 26 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-804296 [75] WPIDS
DOC. NO. CPI: C2003-222129
TITLE: New superantigen binding site within the CD28 molecule, useful for preparing a pharmaceutical composition for **treating** superantigen-related disorders caused by Staphylococcus aureus or Streptococcus pyogenes.
DERWENT CLASS: B04 D16
INVENTOR(S): ARAD, G; KAEMPFER, R
PATENT ASSIGNEE(S): (YISS) YISSUM RES DEV CO HEBREW UNIV JERUSALEM
COUNTRY COUNT: 103
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003084995	A2	20031016	(200375)*	EN	160

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003084995	A2	WO 2003-IL278	20030403

PRIORITY APPLN. INFO: IL 2002-148993 20020404
AN 2003-804296 [75] WPIDS
AB WO2003084995 A UPAB: 20031120
NOVELTY - A superantigen binding site within the CD28 molecule that specifically and directly binds to a superantigen, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a method for **treating** a superantigen-related disorder in a mammalian subject;
(2) a method of **inhibiting** pyrogenic exotoxin-mediated activation of Th1-lymphocytes and protecting against **toxic shock** induced by a pyrogenic exotoxin or by a mixture of pyrogenic exotoxins, in a subject;
(3) a method of eliciting protective immunity against **toxic shock** induced by a pyrogenic exotoxin in a subject;
(4) a substance that **inhibits** the binding of a superantigen to a superantigen binding site in CD28;
(5) a pharmaceutical composition for **treating** or **preventing** superantigen-related disorders comprising the substance that **inhibits** the direct interaction between CD28 molecule and the pyrogenic exotoxin, which leads to antagonizing of toxin-mediated activation of Th1 lymphocytes;
(6) an isolated and purified peptide having an amino acid sequence homologous to an amino acid sequence comprised within a superantigen binding site within the CD28 molecule;
(7) a method of screening for a test substance which specifically binds to the CD28 molecule and is capable of antagonizing pyrogenic exotoxin-mediated activation of Th1 lymphocytes and optionally of eliciting protective immunity against **toxic shock** induced by a pyrogenic exotoxin or by a mixture of at least two pyrogenic exotoxins; and
(8) a method of preparing a **therapeutic** composition for **treating** a superantigen-related disorder in a mammalian subject.
ACTIVITY - Antibacterial.
No biological data given.
MECHANISM OF ACTION - Gene **therapy**.
USE - The substance, peptide or CD28 molecule is useful for preparing a pharmaceutical composition for **treating** superantigen-related disorders caused by Staphylococcus aureus or Streptococcus pyogenes (claimed).
Dwg.0/27

L9 ANSWER 20 OF 26 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-505298 [47] WPIDS
DOC. NO. CPI: C2003-135135
TITLE: New vector, useful for preparing a composition for **treating** or **preventing** bacterial, viral, fungal or parasitic infection.
DERWENT CLASS: B04 C06 D16
INVENTOR(S): FRASER, W D; GALLAGHER, J A; MCCREAVY, D T
PATENT ASSIGNEE(S): (UYLI-N) UNIV LIVERPOOL
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003048371	A2	20030612	(200347)*	EN	52
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW					
AU 2002347346	A1	20030617	(200419)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003048371	A2	WO 2002-GB5512	20021206
AU 2002347346	A1	AU 2002-347346	20021206

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2002347346	A1	Based on	WO 2003048371

PRIORITY APPLN. INFO: GB 2002-23829 20021012; GB 2001-29338 20011207

AN 2003-505298 [47] WPIDS

AB WO2003048371 A UPAB: 20030723

NOVELTY - An vector comprising a heterologous nucleic acid sequence encoding an antigenic polypeptide and a nucleic acid molecule comprising a 3188 base pair sequence, given in the specification, a nucleic acid molecule which hybridizes to it and which encodes a protease **inhibitor** polypeptide, or nucleic acid molecules which comprise degenerate nucleic acid sequences. The vector is adapted for the expression of each polypeptide.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) inducing an immune response to an antigenic polypeptide;

(2) an antibody;

(3) a cell transformed with the novel vector;

(4) producing humanized or chimeric antibody;

(5) a hybridoma cell line which produces a monoclonal antibody;

(6) a vaccine comprising the novel vector; and

(7) vaccinating an animal, preferably a human, against at least one pathological condition.

ACTIVITY - Antibacterial; Virucide; Antiparasitic; Antifungal; Anti-HIV; Antiulcer.

No biological data is given.

MECHANISM OF ACTION - Gene **therapy**; Vaccine.

USE - The vector is useful for preparing a composition for **preventing** or **treating** AIDS, herpes, rubeola, rubella, varicella, influenza, common cold or viral meningitis; septicemia, tuberculosis, bacteria-associated food poisoning, blood infections, peritonitis, endocarditis, sepsis, bacterial meningitis,

pneumonia, stomach ulcers, gonorrhea, strep throat, streptococcal-associated **toxic shock**, necrotizing fasciitis, impetigo, histoplasmosis, Lyme disease, gastro-enteritis, dysentery or shigellosis; Candidiasis; or trypanosomiasis, malaria, schistosomiasis or Chagas disease (claimed).
Dwg.0/9

L9 ANSWER 21 OF 26 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-046760 [04] WPIDS
DOC. NO. CPI: C2003-011859
TITLE: New method of **preventing** or **modulating** T-cell-mediated response in a host, useful for e.g. the **treatment** of **toxic shock** syndrome, comprises administering a Staphylococcus **aureus major histocompatibility complex class II** analog protein.
DERWENT CLASS: B04
INVENTOR(S): BROWN, E; HOOK, M; LEE, L; BROWN, E N; LEE, L Y
PATENT ASSIGNEE(S): (BROW-I) BROWN E; (HOOK-I) HOOK M; (LEEL-I) LEE L; (TEXA) UNIV TEXAS A & M SYSTEM
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002077010	A2	20021003	(200304)*	EN	55
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW					
US 2003108564	A1	20030612	(200340)		
EP 1355662	A2	20031029	(200379)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002077010	A2	WO 2002-US401	20020110
US 2003108564	A1 Provisional	US 2001-260523P	20010110
		US 2002-41775	20020110
EP 1355662	A2	EP 2002-736474	20020110
		WO 2002-US401	20020110

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1355662	A2 Based on	WO 2002077010

Searcher : Shears 571-272-2528

PRIORITY APPLN. INFO: US 2001-260523P 20010110; US 2002-41775 20020110

AN 2003-046760 [04] WPIDS

AB WO 200277010 A UPAB: 20030117

NOVELTY - New method of **preventing** or **modulating** a T-cell-mediated response in a host comprises administering to the host an isolated Staphylococcus **aureus** Map protein, or a composition comprising the S. **aureus major histocompatibility complex class II** analog (Map) protein.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a method of **treating** or **preventing** **pathogenic conditions** associated with overstimulation of **T-cells** in a human or animal patient by administering S. aureus Map protein;

(2) a pharmaceutical composition for **preventing** or **modulating** a T-cell-mediated response to a staphylococcal infection comprising S. aureus Map protein, and a pharmaceutical vehicle, carrier or excipient;

(3) an isolated S. aureus Map protein; and

(4) a method of **treating** or **preventing** a **T-cell** lymphoproliferative **disease** by administering to the host an isolated Map protein selected from Map protein, Map10 protein and Map19 protein.

ACTIVITY - Immunomodulator; Immunosuppressive; Cytostatic.

BALB/c mice were injected in the tail i.v. with 1 multiply 107 Staphylococcus **aureus** (SA), and sacrificed 4 weeks later for histological examination of hind tibiotarsal joints. Preliminary experiments showed that **major histocompatibility complex class II** analog protein (Map)-SA-infected mice had both a reduced frequency and severity of arthritis compared to Map+SA-infected controls. The hypothesis that Map acted as an immunomodulator resulting in impaired immunity to SA with a concomitant inability to respond to a challenge infection was tested by infecting mice with (Map)-SA and Map+SA, respectively, and challenging both groups with Map+SA after 4 weeks. Significant differences were observed in abscess formation in hearts and kidneys between the Map-/Map+-infected groups. Less than 50% of hearts and 25% of kidneys from Map-/Map+ infected mice presented with abscesses compared to more than 75% abscess formation in both hearts and kidneys form Map+/Map+ and -/Map+ infected mice. Significant differences were also observed in arthritis and osteomyelitis scores and frequencies.

MECHANISM OF ACTION - Vaccine.

USE - The major histocompatibility complex class II analog protein (Map) is useful for **preventing** or **modulating** a T-cell-mediated response to a staphylococcal infection, for **treating** or **preventing** **pathogenic conditions** associated with overstimulation of **T-cells** (e.g. **toxic shock** syndrome or **poison ivy**), and lymphoproliferative diseases (claimed).

Dwg.0/5

L9 ANSWER 22 OF 26 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-158657 [16] WPIDS
CROSS REFERENCE: 1991-237984 [32]; 1993-405418 [50]; 1994-302675 [37]; 1998-206533 [18]; 2000-655609 [50]; 2001-380527 [40]; 2002-415198 [41]
DOC. NO. CPI: C2001-046991
TITLE: Tumor cell capable of stimulating antitumor immune reactivity in vitro or in vivo comprises exogenous nucleic acids encoding a superantigen and a costimulatory molecule.
DERWENT CLASS: B04 D16
INVENTOR(S): TERMAN, D S
PATENT ASSIGNEE(S): (TERM-I) TERMAN D S
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6180097	B1	20010130	(200116)*		16

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6180097	B1	CIP of	US 1989-416530	19891003
		CIP of	US 1990-466577	19900117
		CIP of	WO 1991-US342	19910117
		CIP of	US 1992-891718	19920601
		CIP of	US 1993-25144	19930302
		Cont of	US 1994-189424	19940131
		Cont of	US 1995-491746	19950619
			US 1998-183437	19981030

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 6180097	B1	Cont of	US 5728388

PRIORITY APPLN. INFO: US 1994-189424 19940131; US 1989-416530 19891003; US 1990-466577 19900117; WO 1991-US342 19910117; US 1992-891718 19920601; US 1993-25144 19930302; US 1995-491746 19950619; US 1998-183437 19981030
AN 2001-158657 [16] WPIDS
CR 1991-237984 [32]; 1993-405418 [50]; 1994-302675 [37]; 1998-206533 [18]; 2000-655609 [50]; 2001-380527 [40]; 2002-415198 [41]
AB US 6180097 B UPAB: 20020711
NOVELTY - Tumor cell capable of stimulating antitumor immune reactivity in vitro or in vivo contains and expresses an exogenous nucleic acid molecule encoding a superantigen or its active fragment and an exogenous nucleic acid molecule encoding a costimulatory molecule that activates T cells in conjunction with an antigenic

stimulus.

ACTIVITY - Cytostatic; immunostimulant.

Eight to twelve week old female C57BL/W (B6) mice were injected intravenously (i.v.) with approximately 300000 MCA 205 tumor cells (i.e., methylcholanthrene-induced tumors of B6 origin) suspended in 1 ml of media to initiate pulmonary metastases. These tumors can be routinely passed in vivo in syngeneic mice and used within the third to seventh transplantation generation.

On day 3, cells obtained from the mice were stimulated ex vivo. Specifically, LN cells draining progressively growing MCA 205 fibrosarcoma for 12 days were stimulated with graded concentrations of staphylococcal enterotoxin A (SEA) or SEB for 2 days followed by culture in 4 U/ml of interleukin-2 (IL-2) for 3 days.

The antitumor efficacy of superantigen stimulated cells was assessed by reinfusion. Mice may also be **treated** with exogenous IL-2 to promote the growth of transferred cells (intraperitoneally with 15000 Units IL-2 in 0.5 ml buffered saline twice daily for 4 consecutive days to promote the in vivo function and survival of the stimulated cells). On day 20 or 21, all mice were randomized, sacrificed, and metastatic tumor nodules on the surface of the lungs enumerated. No results are given.

MECHANISM OF ACTION - None given.

USE - For cancer **therapy** by stimulating an anticancer immune response in vivo or ex vivo.

ADVANTAGE - The tumor cells can **treat** solid tumors including their metastases, without radiation, surgery or standard chemotherapeutic agents.

Dwg.0/2

L9 ANSWER 23 OF 26 JICST-EPlus COPYRIGHT 2004 JST on STN

ACCESSION NUMBER: 990321141 JICST-EPlus

TITLE: Atopic Dermatitis and Staphylococcus aureus. Staphylococcal Exotoxins as Superantigens: Cutaneous **Conditions** That Evoke **T-cell** Responses to Superantigenic Toxins.

AUTHOR: TOKURA YOSHIKI

CORPORATE SOURCE: Hamamatsu Univ. Sch. of Med.

SOURCE: Hifu (Skin Research), (1998) vol. 40, no. Suppl.20, pp. 32-38. Journal Code: Z0014B (Fig. 3, Tbl. 2, Ref. 22)
ISSN: 0018-1390

PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

STATUS: New

AB Bacterial exotoxins that stimulate T cells in a T-cell receptor V B-restricted manner are collectively termed as superantigens. Staphylococcus **aureus**(S.**aureus**) and Streptococcus pyogenes are the major bacteria that produce superantigens. Skin-colonization with S.**aureus** is one of the factors for exacerbation of several skin disorders. It is suggested that this effect of S.**aureus** is mediated by activation of lesional T cells with released superantigens. In skin milieu, not only Langerhans cells but also **MHC class II**-bearing keratinocytes can function as accessory cells in T-cell responses to superantigens. Furthermore,

bacterial superantigens stimulate keratinocytes to produce cytokines such as tumor necrosis factor A and to augment the expression of CD54. In vitro studies can be performed to address how T cells are stimulated by superantigen-releasing S.**aureus** in the presence of keratinocytes, when mitomycin C(MMC)-**treated** S.**aureus**, that are unable to propagate but retain their ability to produce superantigens, are used as stimulants. When purified T cells are cultured with MMC-**treated** S.**aureus** or supernatant in the presence of interferon-Γ-pretreated kerationcytes, the supernatant, but not MMC-**treated** S.**aureus**, is capable of stimulating T cells. Keratinocytes are highly susceptible to A-toxin compared with monocytes and B cells functioning as accessory cells in PBMC. Therefore, no response of T cells to S.**aureus** plus keratinocytes is thought to be due to damage of superantigen-presenting function of keratinocytes by cytolysin. The activity of A-toxin is much less stable than that of superantigen during incubation. Given that S.**aureus** -colonized skin provides circumstances in which viable keratinocytes are exposed to excreted superantigens but not to active cytolysin (s), skin-infiltrating T cells may be effectively stimulated by S.**aureus**. (author abst.)

L9 ANSWER 24 OF 26 JICST-EPlus COPYRIGHT 2004 JST on STN

ACCESSION NUMBER: 950445837 JICST-EPlus

TITLE: Proliferative Response and Cytokine Production of Bovine Peripheral Blood Mononuclear Cells Induced by the Superantigens Staphylococcal Enterotoxins and **Toxic Shock** Syndrome Toxin-1.

AUTHOR: YOKOMIZO Y; MORI Y; SHIMOJI Y; SHIMIZU S
SENTSUI H; KODAMA M
IGARASHI H

CORPORATE SOURCE: National Inst. Animal Health, Ibaraki, JPN
National Inst. Animal Health, Sapporo, JPN
Tokyo Metropolitan Res. Lab. Public Health, Tokyo, JPN

SOURCE: J Vet Med Sci, (1995) vol. 57, no. 2, pp. 299-305.
Journal Code: F0905A (Fig. 4, Ref. 33)
ISSN: 0916-7250

PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Article

LANGUAGE: English

STATUS: New

AB The potential of staphylococcal enterotoxin A (SEA), B (SEB), C (SEC) and **toxic shock** syndrome toxin-1 (TSST-1) to act as superantigens by inducing polyclonal T-cell mitogenesis and cytokine production was tested on bovine peripheral blood mononuclear cells (PBMC). These four toxins were capable of inducing strong proliferative response of PBMC from calves over a broad dosage range (1 Pg/ml to 1 Mg/ml) in vitro. The toxin-activated blast cells consisted of both CD4+ T-cells and CD8+ T-cells, but the T-cell proliferation depended upon the presence of monocytes. **Treatment** of monocytes with monoclonal antibody to **major histocompatibility complex class II** antigens substantially **inhibited** the toxin-induced T-cell proliferative response, but

paraformaldehyde-fixation did not abrogate the accessory function. SEA, SEB, SEC and TSST-1, all induced the in vitro release of interleukin-2, interferon Γ and tumor necrosis factor A in a dose dependent manner. The results indicate that SEA, SEB, SEC and TSST-1 are capable of acting as superantigens by stimulating bovine T-cells as shown in the human and murine systems. The possible implications of these toxins in the immunopathogenesis of bovine mastitis caused by the infection with Staphylococcus **aureus** are discussed. (author abst.)

L9 ANSWER 25 OF 26 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002-0119480 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2002 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Use of intravenous immunoglobulin in the **treatment** of staphylococcal and streptococcal **toxic shock** syndromes and related illnesses
Immunoglobulin **Therapy**: Dynamic New Directions for Biological and Clinical Applications
AUTHOR: SCHLIEVERT Patrick M.
SACHER Ronald A. (ed.)
CORPORATE SOURCE: Department of Microbiology, University of Minnesota Medical School, Minneapolis, Minn., United States
Internal Medicine and Pathology, University of Cincinnati MedicBl Center, Cincinnati, Ohio, United States
Bayer Corp., Research Triangle Park, NC, United States (patr.)
SOURCE: Journal of allergy and clinical immunology, (2001), 108(4, SUP), S107-S110, 12 refs.
Conference: IVIG Advisory Meeting 2000, Santa Barbara, California (United States), 26 Oct 2000
ISSN: 0091-6749 CODEN: JACIBY
DOCUMENT TYPE: Journal; Conference
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-2059, 354000099822580060
AN 2002-0119480 PASCAL
CP Copyright .COPYRGT. 2002 INIST-CNRS. All rights reserved.
AB Pyrogenic toxin superantigens comprise a large family of exotoxins made by Staphylococcus **aureus** and group A streptococci. These toxins include **toxic shock** syndrome toxin-1, the staphylococcal enterotoxins, and the streptococcal pyrogenic exotoxins (synonyms: scarlet fever toxins and erythrogenic toxins), all of which have the ability to cause **toxic shock** syndromes and related illnesses. These toxins have a similar three-dimensional structure that allows them to interact with relatively invariant regions of **major histocompatibility complex class II** molecules on the surface of antigen-presenting cells and with certain variable regions of the T-cell receptor-β chain.

The consequence of these interactions (and other immunobiological properties of the toxins) is the exaggerated release of bioactive cytokines. The latter molecules are responsible for the clinical signs of illness associated with these toxins.

L9 ANSWER 26 OF 26 DISSABS COPYRIGHT (C) 2004 ProQuest Information and Learning Company; All Rights Reserved on STN

ACCESSION NUMBER: 96:42943 DISSABS Order Number: AAI9621792
TITLE: STRUCTURE-FUNCTION ANALYSIS OF THE SUPERANTIGEN STAPHYLOCOCCAL ENTEROTOXIN C1 BY MUTAGENESIS (STAPHYLOCOCCUS AUREUS, STREPTOCOCCUS PYOGENES, **TOXIC SHOCK**)
AUTHOR: HOFFMANN, MARCY LYNN [PH.D.]; BOHACH, GREGORY A. [advisor]
CORPORATE SOURCE: UNIVERSITY OF IDAHO (0089)
SOURCE: Dissertation Abstracts International, (1995) Vol. 57, No. 3B, p. 1602. Order No.: AAI9621792. 178 pages.
DOCUMENT TYPE: Dissertation
FILE SEGMENT: DAI
LANGUAGE: English
ENTRY DATE: Entered STN: 19960807
Last Updated on STN: 19960807

AB Staphylococcal enterotoxin C1 (SEC1) belongs to a large family of related pyrogenic toxins (PTs) produced by Staphylococcus **aureus** and Streptococcus pyogenes. The PTs share biological properties including pyrogenicity, mitogenicity, immunosuppression, cytokine induction and enhancement of lethal endotoxin shock. Many of these activities have been implicated in the pathogenesis of **toxic shock** syndrome (**TSS**) and streptococcal **toxic shock** syndrome (STSS). The molecular mechanisms attributed to biological activity are not completely understood. The PTs also exhibit four regions of primary sequence similarity which we theorize are responsible for shared biological properties. To investigate mechanisms of PT action and the role of shared primary sequences in these mechanisms, we assessed the effects of various mutations on the function of SEC1. A series of deletion mutants were produced near the N-terminus of SEC1. In addition, site-directed mutants were generated by substituting selected highly conserved residues. Mutants with deletions occurring between residues 6 through 13 did not lose mitogenic activity while deletions between positions 19 through 33 completely abolished activity. Nonmitogenic mutants **inhibited** T cell proliferation induced by SEC1. Flow cytometric analysis of toxin-stimulated peripheral blood mononuclear cell (PBMC) cultures reconfirmed results from T cell proliferation assays. Loss of mitogenic activity could not be attributed to reduced binding to **major histocompatibility complex (MHC) class II** molecules on Raji cells. These data indicate that deletions in nonmitogenic mutants occur within a region that interacts with the Vβ portion of the T cell receptor (TCR). Mutants tested in the rabbit shock model dissociated T cell proliferation from the activities of toxicity and pyrogenicity. Alanine substitutions at positions 83, 151, 157 and 158 did not eliminate the mitogenic capacity of SEC1. Mutant E158A exhibited the greatest loss in mitogenic activity. All mutants could efficiently compete with SEC1

for binding sites on **MHC class II**,
suggesting that residues 83, 151, 157 and 158 do not directly interact with this receptor. Localization of biologically important regions of the PTs will facilitate the production of a vaccine protective against classic **TSS** and the related disease, STSS.

(FILE 'MEDLINE' ENTERED AT 15:51:53 ON 30 APR 2004)

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L10        9474 SEA FILE=MEDLINE ABB=ON  PLU=ON  "MAJOR HISTOCOMPATIBILIT
                Y COMPLEX"/CT
L11         194 SEA FILE=MEDLINE ABB=ON  PLU=ON  TOXICODENDRON/CT
L12       12144 SEA FILE=MEDLINE ABB=ON  PLU=ON  "SHOCK, SEPTIC"/CT
L13           4 SEA FILE=MEDLINE ABB=ON  PLU=ON  L10 AND (L11 OR L12)
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L13 ANSWER 1 OF 4 MEDLINE on STN

ACCESSION NUMBER: 2003457712 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14519947
TITLE: Alleviation of experimental septic shock in mice by acidic polysaccharide isolated from the medicinal mushroom Phellinus linteus.
AUTHOR: Kim Gi-Young; Roh Su-In; Park Soon-Kew; Ahn Soon-Cheol; Oh Yang-Hyo; Lee Jae-Dong; Park Yeong-Min
CORPORATE SOURCE: Department of Microbiology, College of Natural Sciences, Pusan National University, South Korea.
SOURCE: Biological & pharmaceutical bulletin, (2003 Oct) 26 (10) 1418-23.
Journal code: 9311984. ISSN: 0918-6158.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20031002
Last Updated on STN: 20040218
Entered Medline: 20040217

ED Entered STN: 20031002
Last Updated on STN: 20040218
Entered Medline: 20040217

AB This study reports that acidic polysaccharide (PL) isolated from Phellinus linteus alleviated the septic shock induced by high dose lipopolysaccharide (LPS) injection in mice. To examine the origin of this effect, we investigated cytokine production in serum and the expression of MHC II in B cells and macrophages in areas of inflammation. Pretreatment with PL 24 h before LPS administration resulted in a significant inhibition of up to 68% of circulating tumor necrosis factor (TNF)-alpha, a moderate reduction of 45% of interleukine (IL)-12 and 23% of IL-1beta, but no significant reduction in IL-6. In addition, the expression of MHC II in B cells and macrophages was examined. Our results show that LPS-stimulated cytokine release and the level of MHC II can be modulated by in vivo administration of soluble PL in mice. The decrease of IL-1beta, IL-12 and TNF-alpha in sera and the down-modulation of MHC II during septic shock may contribute to the long survival of mice by PL. Administration of PL in vivo decreases IL-2, IFN-gamma and TNF-alpha production in splencotyes and enhances spontaneous cell apoptosis in macrophages and lymphocytes stimulated with LPS in vitro. Thus,

part of the anti-inflammatory effects of PL treatment in vivo may result from the enhanced apoptosis of a portion of the activated macrophages and lymphocytes. The ability of PL to significantly reduce the TNF-alpha production indicates the potential of the polysaccharides in possible therapeutic strategies that are based on down-regulation of TNF-alpha.

L13 ANSWER 2 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2003393381 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12930353
TITLE: Bacterial superantigens.
AUTHOR: Proft T; Fraser J D
CORPORATE SOURCE: School of Medical Sciences, University of Auckland, Auckland New Zealand.
SOURCE: Clinical and experimental immunology, (2003 Sep) 133 (3) 299-306. Ref: 75
Journal code: 0057202. ISSN: 0009-9104.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 20030822
Last Updated on STN: 20031015
Entered Medline: 20031014
ED Entered STN: 20030822
Last Updated on STN: 20031015
Entered Medline: 20031014

L13 ANSWER 3 OF 4 MEDLINE on STN
ACCESSION NUMBER: 95020776 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7935042
TITLE: Bacterial superantigens--mechanism of T cell activation by the superantigens and their role in the pathogenesis of infectious diseases.
AUTHOR: Uchiyama T; Yan X J; Imanishi K; Yagi J
CORPORATE SOURCE: Department of Microbiology and Immunology, School of Medicine, Tokyo Women's Medical College, Japan.
SOURCE: Microbiology and immunology, (1994) 38 (4) 245-56. Ref: 86
Journal code: 7703966. ISSN: 0385-5600.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19941222
Entered Medline: 19941115
ED Entered STN: 19941222
Last Updated on STN: 19941222
Entered Medline: 19941115

Searcher : Shears 571-272-2528

L13 ANSWER 4 OF 4 MEDLINE on STN
ACCESSION NUMBER: 93275263 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8502189
TITLE: [Superantigens and antigen recognition of T lymphocytes].
Superantijenler ve T lenfositlerinin antijeni tanimasi.
AUTHOR: Gulmezoglu E
CORPORATE SOURCE: Ankara Mikrobiyoloji Dernegi Bilimsel Toplantisinda sunulmustur.
SOURCE: Mikrobiyoloji bulteni, (1993 Apr) 27 (2) 164-70.
Ref: 10
Journal code: 7503830. ISSN: 0374-9096.
PUB. COUNTRY: Turkey
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Turkish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199306
ENTRY DATE: Entered STN: 19930716
Last Updated on STN: 19930716
Entered Medline: 19930630

ED Entered STN: 19930716
Last Updated on STN: 19930716
Entered Medline: 19930630

AB Superantigens are antigens which can stimulate T cells bound to MHC molecules. The conventional foreign antigens are recognized by the T cell within the MHC peptide binding groove. Superantigens differ from conventional antigens. They bind with high affinity to class II MHC molecules outside the antigen binding groove in the absence of antigen processing. The MHC class II/superantigen complexes on antigen presenting cells trigger the proliferation of T cells expressing the TcR-VB gene products. Superantigens can amplify or suppress immune responses. To date, two main groups of superantigens have been described, namely endogenous and exogenous superantigens. Exogenous superantigens are microbial toxins and other protein products. Endogenous superantigens are the products of unlinked genetic loci in mice the best known of which are the murine retroviral gene products. Toxins of S. aureus and S. pyogenes are the best known exogenous superantigens, implicated in Toxic Shock Syndrome.

(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER, PASCAL, DISSABS, FEDRIP' ENTERED AT 15:53:11 ON 30 APR 2004)

L14 14113 S "BROWN E"?/AU
L15 14144 S "LEE L"?/AU
L16 1137 S "HOOK M"?/AU
L17 10 S L14 AND L15 AND L16
L18 37 S L14 AND (L15 OR L16)
L19 10 S L15 AND L16
L20 11 S (L18 OR L14 OR L15 OR L16) AND L5
L21 16 S L17 OR L19 OR L20
L22 6 DUP REM L21 (10 DUPLICATES REMOVED)

Author (s)

Searcher : Shears 571-272-2528

L22 ANSWER 1 OF 6 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2003375258 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12761224
TITLE: Decorin-binding sites in the adhesin DbpA from Borrelia burgdorferi: a synthetic peptide approach.
AUTHOR: Pikas Dagmar Sandback; **Brown Eric L**; Gurusiddappa Sivashankarappa; **Lee Lawrence Y**; Xu Yi; **Hook Magnus**
CORPORATE SOURCE: Center for Extracellular Matrix Biology, Albert B. Alkek Institute of Biosciences and Technology, Texas A&M University Health Science Center, Houston, Texas 77030, USA.
CONTRACT NUMBER: AR-44415 (NIAMS)
CCU618387 (CDC)
SOURCE: Journal of biological chemistry, (2003 Aug 15) 278 (33) 30920-6.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200311
ENTRY DATE: Entered STN: 20030812
Last Updated on STN: 20031111
Entered Medline: 20031110

AB Lyme disease is caused by the spirochete Borrelia burgdorferi following transmission from infected Ixodes ticks to human hosts. Following colonization of the skin, spirochetes can disseminate throughout the body, resulting in complications that can include ocular, cardiac, neural, and skeletal disease. We have previously shown that B. burgdorferi expresses two closely related decorin-binding adhesins (DbpA and DbpB) of the MSCRAMM (microbial surface component recognizing adhesive matrix molecule) type that can mediate bacterial attachment to extracellular matrices in the host. Furthermore, three Lys residues in DbpA appear to be critical for the binding of DbpA to decorin. We have now characterized the interaction of DbpA and decorin further by using a synthetic peptide approach. We synthesized a panel of peptides that spanned the DbpA sequence and examined their ability to inhibit the binding of intact DbpA to decorin. From these studies, we identified a decorin-binding peptide that lost this activity if the sequence was either scrambled or if a critical Lys residue was chemically modified. A minimal decorin-binding peptide was identified by examining a set of truncated peptides. One peptide is proposed to contain the primary decorin-binding site in DbpA. By comparing the amino acid sequences of 29 different DbpA homologs from different B. burgdorferi sensu lato isolates, we discovered that the identified decorin-binding sequence was quite variable. Therefore, we synthesized a new panel of peptides containing the putative decorin-binding sequence of the different DbpA homologs. All of these peptides were active in our decorin-binding assay, and consensus decorin binding motifs are discussed.

L22 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2002:754410 HCAPLUS

DOCUMENT NUMBER: 137:277779
TITLE: Method of preventing T cell-mediated responses by the use of the **major histocompatibility complex class II** analog protein (Map protein) from Staphylococcus **aureus**
INVENTOR(S): **Brown, Eric N.; Lee, Lawrence Y.; Hook, Magnus**
PATENT ASSIGNEE(S): The Texas A & M University System, USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002077010	A2	20021003	WO 2002-US401	20020110
WO 2002077010	C2	20021114		
WO 2002077010	A3	20030403		
WO 2002077010	C1	20031113		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003108564	A1	20030612	US 2002-41775	20020110
EP 1355662	A2	20031029	EP 2002-736474	20020110

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 2001-260523P P 20010110
WO 2002-US401 W 20020110

AB A method of immunomodulating the T cell response in Staphylococcal bacteria is provided wherein an effective amount of the Map protein from Staphylococcus aureus is administered to a host to prevent or suppress the T cell response. The present method may be utilized with either the Map protein or an effective subdomain of a fragment thereof such as the Map10 or Map19 protein. The present invention is advantageous in that suppression or prevention of the T cell response in a host can prevent or ameliorate a wide variety of the pathogenic conditions such as T cell lymphoproliferative disease and toxic shock syndrome wherein the overstimulation of T cell needs to be suppressed or modulated.

L22 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2002:897499 HCAPLUS
DOCUMENT NUMBER: 138:3644
TITLE: The Staphylococcus aureus Map protein is an immunomodulator that interferes with T

cell-mediated responses

AUTHOR(S): **Lee, Lawrence Y.**; Miyamoto, Yuko J.; McIntyre, Bradley W.; **Hook, Magnus**; McCrea, Kirk W.; McDevitt, Damien; **Brown, Eric L.**

CORPORATE SOURCE: The Center for Extracellular Matrix Biology, Albert B. Alkek Institute of Biosciences and Technology, Texas A and M University System Health Science Center, Houston, TX, 77030-7552, USA

SOURCE: Journal of Clinical Investigation (2002), 110(10), 1461-1471
CODEN: JCINAO; ISSN: 0021-9738

PUBLISHER: American Society for Clinical Investigation

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Staphylococcus aureus (SA) is an opportunistic pathogen that affects a variety of organ systems and is responsible for many diseases worldwide. SA express an MHC class II analog protein (Map), which may potentiate SA survival by modulating host immunity. The authors tested this hypothesis in mice by generating Map-deficient SA (Map-SA) and comparing disease outcome to wild-type Map-SA-infected mice. Map-SA-infected mice presented with significantly reduced levels of arthritis, osteomyelitis, and abscess formation compared with control animals. Furthermore, Map-SA-infected nude mice developed arthritis and osteomyelitis to a severity similar to Map+SA-infected controls, suggesting that T cells can affect disease outcome following SA infection and Map may attenuate cellular immunity against SA. The capacity of Map to alter T cell function was tested more specifically in vitro and in vivo using native and recombinant forms of Map. T cells or mice treated with recombinant Map had reduced T cell proliferative responses and a significantly reduced delayed-type hypersensitivity response to challenge antigen, resp. These data suggest a role for Map as an immunomodulatory protein that may play a role in persistent SA infections by affecting protective cellular immunity.

REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 4 OF 6 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 2000-256496 [22] WPIDS

DOC. NO. CPI: C2000-078210

TITLE: Immunizing patients to treat staphylococcal infections comprises administering immunoglobulins having higher antibody titer to staphylococcal adhesin protein.

DERWENT CLASS: B04 D16

INVENTOR(S): FOSTER, T J; **HOOK, M**; PATTI, J M

PATENT ASSIGNEE(S): (INHI-N) INHIBITEX INC; (QUEE-N) QUEEN ELIZABETH COLLEGE DUBLIN; (TEXA) UNIV TEXAS A & M SYSTEM; (FOST-I) FOSTER T J; (HOOK-I) HOOK M; (PATT-I) PATTI J M

COUNTRY COUNT: 89

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000012132	A1	20000309	(200022)*	EN	84
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW					
AU 9956966	A	20000321	(200031)		
NO 2001000981	A	20010426	(200131)		
EP 1121149	A1	20010808	(200146)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2002523474	W	20020730	(200264)		88
US 2002159997	A1	20021031	(200274)		
AU 762978	B	20030710	(200355)		
US 6692739	B1	20040217	(200413)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000012132	A1	WO 1999-US19729	19990831
AU 9956966	A	AU 1999-56966	19990831
NO 2001000981	A	WO 1999-US19729	19990831
		NO 2001-981	20010227
EP 1121149	A1	EP 1999-943981	19990831
		WO 1999-US19729	19990831
JP 2002523474	W	WO 1999-US19729	19990831
		JP 2000-567243	19990831
US 2002159997	A1 Provisional	US 1998-98449P	19980831
	Div ex	US 1999-386960	19990831
		US 2002-91494	20020307
AU 762978	B	AU 1999-56966	19990831
US 6692739	B1 Provisional	US 1998-98449P	19980831
		US 1999-386960	19990831

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9956966	A	Based on	WO 2000012132
EP 1121149	A1	Based on	WO 2000012132
JP 2002523474	W	Based on	WO 2000012132
AU 762978	B	Previous Publ.	AU 9956966
		Based on	WO 2000012132

PRIORITY APPLN. INFO: US 1998-98449P 19980831; US 1999-386960 19990831; US 2002-91494 20020307

AN 2000-256496 [22] WPIDS

AB WO 200012132 A UPAB: 20021105

NOVELTY - Immunizing patients to treat or prevent staphylococcal infection comprises administering immunologically effective amount of purified immunoglobulins (IG) obtained by treating donor plasma

(I) having higher antibody (Ab) titer to staphylococcal adhesin.

DETAILED DESCRIPTION - Immunizing patients to treat or prevent staphylococcal infections comprising:

(a) providing a source of donor plasma having a higher than normal antibody titer to a staphylococcal adhesin;

(b) treating the donor plasma to obtain purified immunoglobulin; and

(c) administering to the patient an immunologically effective amount of purified immunoglobulin-containing donor plasma.

INDEPENDENT CLAIMS are also included for the following:

(1) method of obtaining (I) comprises recovering plasma from the blood sample having higher Ab titer to staphylococcal adhesin and treating the donor plasma to obtain IG in a purified state that has higher Ab titer to staphylococcal adhesin;

(2) a donor plasma composition obtained by the method (2); and

(3) a kit (II) for identification of blood or plasma having higher titers of Ab comprises an antigen to a staphylococcal Ab, a support to bind the antigen and a detectable label that can be attached to the Ab.

ACTIVITY - Antibacterial; vulnerary. The effect of SA-IVIG MS502 (S) in the treatment of staphylococcal infection was tested using mice 5-6 weeks old. The animals were injected with 5.6 multiply 107 CFU Staphylococcus aureus (SA) 601 via the tail vein. The next day the animals were treated with single 0.5 ml intraperitoneal injection of (S). Control mice were left untreated. The mice were followed up for 5 days and were then sacrificed. The results showed that 93% of the mice that received (S) prior to SA challenge survived whereas only 76 % of the control mice survived the bacterial challenge, clearly indicating that the administration of ClfA donor selected human SA-IVIG provided a significant and effective treatment of staphylococcal infections.

MECHANISM OF ACTION - Vaccine.

USE - The method is useful for treating staphylococcal infections (claimed) and thereby treats mastitis, arthritis, endocarditis, septicemia, osteomyelitis, furunculosis, cellulitis, pyemia, pneumonia, pyoderma, suppuration of wounds, food poisoning and bladder infections. (II) is useful for identifying blood or plasma having higher antibody titers to staphylococcal adhesin (claimed).

ADVANTAGE - The method is useful for treating wide variety of staphylococcal infections.

Dwg.0/2

L22 ANSWER 5 OF 6 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 1997-372059 [34] WPIDS

DOC. NO. CPI: C1997-119824

TITLE: DNA encoding Staphylococcus aureus broad spectrum adhesin - for production of recombinant adhesin for use in vaccines.

DERWENT CLASS: B04 D16

INVENTOR(S): GURUSIDDAPPA, S; **HOOK, M**; JONSSON, K; PATTI, J M

PATENT ASSIGNEE(S): (TEXA) UNIV TEXAS A & M

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5648240	A	19970715	(199734)*		30

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5648240	A	US 1994-248021	19940524

PRIORITY APPLN. INFO: US 1994-248021 19940524
AN 1997-372059 [34] WPIDS
AB US 5648240 A UPAB: 19970820
Novel DNA segment comprises an isolated gene encoding a Staphylococcus **aureus** broad spectrum adhesin capable of binding fibronectin or vitronectin, having a molecular weight of about 70 kD (by SDS-PAGE) and comprising a **major histocompatibility complex type II** (**MHC** II) mimicking unit of about 30 residues.
Also claimed are: (1) recombinant vector comprising the DNA segment; (3) recombinant host cell transformed with the vector; and (4) composition comprising a protein or peptide encoded by the DNA segment and an excipient.
USE - The DNA segment can be used to produce a MHC II antigen protein analogue, while the composition can be used to induce an immune response in an animal, especially inducing an immune response to S. aureus in an individual suspected of being susceptible to, or having a staphylococcal infection.
Dwg.0/5

L22 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1995:812072 HCAPLUS
DOCUMENT NUMBER: 123:333097
TITLE: Staphylococcus **aureus** expresses a **major histocompatibility complex class II** analog
AUTHOR(S): Joensson, Klas; McDevitt, Damien; McGavin, Mary Homonylo; Patti, Joseph M.; **Hook, Magnus**
CORPORATE SOURCE: Cent. Extracellular Matrix Biol. Dep. Biochem. Biophys., Inst. Biosci. Technol., Texas A & M Univ., Houston, TX, 77030-3303, USA
SOURCE: Journal of Biological Chemistry (1995), 270(37), 21457-60
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Bio logy
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Staphylococcus aureus expresses various surface proteins which specifically recognize and bind to different host mols. We have previously identified a bacterial protein that exhibits a broad specificity and binds to several mammalian extracellular proteins. The gene encoding this bacterial component has now been cloned and sequenced. The deduced protein consists predominantly of six

repeated domains of 110 residues. Each of the repeated domains contain a subdomain of 31 residues that share striking sequence homol. with a segment in the peptide binding groove of the β chain of the major histocompatibility complex (MHC) class II proteins from different mammalian species. The purified recombinant bacterial protein bound several mammalian proteins, including recombinant osteopontin, suggesting a protein-protein interaction and also specifically recognized a 15-amino acid residue synthetic peptide. Taken together, these results suggest that the bacterial protein resembles mammalian MHC class II mols. with respect to both sequence similarities and peptide binding capabilities.

FILE 'HOME' ENTERED AT 15:55:39 ON 30 APR 2004

Devi, S.
10/041775

30apr04 14:59:21 User219783 Session D2013.2

SYSTEM:OS - DIALOG OneSearch
File 65:Inside Conferences 1993-2004/Apr W4
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File 348:EUROPEAN PATENTS 1978-2004/Apr W04
(c) 2004 European Patent Office
File 357:Derwent Biotech Res. 1982-2004/May W1
(c) 2004 Thomson Derwent & ISI
File 113:European R&D Database 1997
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-key terms

Set Items Description
S1 102 (MAP19 OR MAP(W)19 OR (MHC OR MAJOR(W)(HISTOCOMPATIB? OR H-ISTO(W)COMPATIB?)(W)COMPLEX)(5N)((CLASS OR TYPE)(W)(II OR 2)) OR MHCII)(S)AUREUS
S2 36 S1 AND ((TOXIC OR SEPTIC OR ENDOTOXIC)(W)SHOCK OR POISON(W-)IVY OR TSS OR TOXICODENDRON OR TOXICO(W)DENDRON OR (T(W)(CELL OR LYMPHOCYT?) OR PATHOGENIC?)(5N)(DISEAS? OR DISORDER?? OR CONDITION? ?))
S3 36 RD (unique items)
>>>No matching display code(s) found in file(s): 65, 113

3/3,AB/1 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
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18178046 Document Delivery Available: 000220485800001 References: 89
TITLE: Interplay between superantigens and immunoreceptors
AUTHOR(S): Petersson K; Forsberg G; Walse B (REPRINT)
AUTHOR(S) E-MAIL: bjorn.walse@activebiotech.com
CORPORATE SOURCE: Act Biotech Res AB, POB 724/S-22007 Lund//Sweden/ (REPRINT); Act Biotech Res AB, /S-22007 Lund//Sweden/
PUBLICATION TYPE: JOURNAL
PUBLICATION: SCANDINAVIAN JOURNAL OF IMMUNOLOGY, 2004, V59, N4 (APR), P 345-355
GENUINE ARTICLE#: 807EW
PUBLISHER: BLACKWELL PUBLISHING LTD, 9600 GARSINGTON RD, OXFORD OX4 2DG, OXON, ENGLAND
ISSN: 0300-9475
LANGUAGE: English DOCUMENT TYPE: REVIEW

ABSTRACT: Superantigens (SAGs) cause a massive T-cell proliferation by simultaneously binding to major histocompatibility complex (MHC) class II on antigen-presenting cells and T-cell receptors (TCRs) on T cells. These **T-cell** mitogens can cause **disease** in host, such as food poisoning or **toxic shock**. The best characterized groups of SAGs are the bacterial SAGs secreted by Staphylococcus **aureus** and Streptococcus pyogenes. Despite a common overall three-dimensional fold of these SAGs, they have been shown to bind to **MHC class II** in different ways. Recently, it has also been shown that SAGs have

individual preferences in their binding to the TCRs. They can interact with various regions of the variable beta-chain of TCRs and at least one SAG seems to bind to the alpha-chain of TCRs. In this review, different subclasses of SAGs are classified based upon their binding mode to **MHC class II**, and models of trimolecular complexes of MHC-SAG-TCR molecules are described in order to reveal and understand the complexity of SAG-mediated T-cell activation.

3/3,AB/2 (Item 2 from file: 440)

17860875 Document Delivery Available: 000188776500079 References: 39
TITLE: Design of chimeric receptor mimics with different TcRV beta isoforms - Type-specific inhibition of superantigen pathogenesis
AUTHOR(S): Hong-Geller E; Mollhoff M; Shiflett PR; Gupta G (REPRINT)
AUTHOR(S) E-MAIL: gxg@lanl.gov
CORPORATE SOURCE: Los Alamos Natl Lab, Biosci Div, HRL-1,MS-M888/Los Alamos//NM/87544 (REPRINT); Los Alamos Natl Lab, Biosci Div, /Los Alamos//NM/87544
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF BIOLOGICAL CHEMISTRY, 2004, V279, N7 (FEB 13), P 5676-5684
GENUINE ARTICLE#: 771GD
PUBLISHER: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA
ISSN: 0021-9258
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Staphylococcus aureus enterotoxins (S.E.) A-I, and **toxic-shock** syndrome toxin TSST-1 act as superantigens to cause overstimulation of the host immune system, leading to the onset of various diseases including food poisoning and **toxic shock** syndrome. SAgs bind as intact proteins to the DRalpha1 domain of the **MHC class II** receptor and the TcRVbeta domain from the T cell receptor and cause excessive release of cytokines such as IL-2, TNF-alpha, and IFN-gamma, and hyperproliferation of T cells. In addition, different SAgs bind and activate different TcRVbeta isoforms during pathogenesis of human immune cells. These two properties of SAgs prompted us to design several chimeric DRalpha1-linker-TcRVbeta proteins using different TcRVbeta isoforms to create chimeras that would specifically inhibit the pathogenesis of SAgs against which they were designed. In this study, we compare the design, interaction, and inhibitory properties of three different DRalpha1-linker-TcRVbeta chimeras targeted against three different SAgs, SEB, SEC3, and TSST-1. The inhibitory properties of the chimeras were tested by monitoring IL-2 release and T cell proliferation using a primary human cell model. We demonstrate that the three chimeras specifically inhibit the pathogenesis of their target superantigen. We performed molecular modeling to analyze the structural basis of the type specificity exhibited by different chimeras designed against their target SAgs, examine the role of the linker in determining binding and specificity, and suggest site-specific mutations in the chimera to enhance binding affinity. The fact that our strategy works equally well for SEB and TSST-1, two widely different phylogenic variants, suggests that the DRalpha1-linkerTcRVbeta chimeras may be developed as a general therapy

against a broad spectrum of superantigens released during Staphylococcal infection.

3/3,AB/3 (Item 3 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

15750109 Document Delivery Available: 000181489500003 References: 104
TITLE: Staphylococcal and streptococcal superantigens: molecular, biological and clinical aspects
AUTHOR(S): Alouf JE (REPRINT); Muller-Alouf H
AUTHOR(S) E-MAIL: joseph.alouf@wanadoo.fr
CORPORATE SOURCE: Domaine Ronce 7,Av Cedres, /F-92410 Villedavray//France/ (REPRINT); Inst Pasteur, /F-75724 Paris 15//France/
PUBLICATION TYPE: JOURNAL
PUBLICATION: INTERNATIONAL JOURNAL OF MEDICAL MICROBIOLOGY, 2003, V292, N7-8 (FEB), P429-440
GENUINE ARTICLE#: 654HM
PUBLISHER: URBAN & FISCHER VERLAG, BRANCH OFFICE JENA, P O BOX 100537, D-07705 JENA, GERMANY
ISSN: 1438-4221
LANGUAGE: English DOCUMENT TYPE: REVIEW

ABSTRACT: Superantigens (SAgs) include a class of certain bacterial and viral proteins exhibiting highly potent lymphocyte-transforming (mitogenic) activity towards human and or other mammalian T lymphocytes. Unlike conventional antigens, SAgs bind to certain regions of major histocompatibility complex (MHC) class II molecules of antigen-presenting cells (APCs) outside the classical antigen-binding groove and concomitantly bind in their native form to T cells at specific motifs of the variable region of the beta chain (Vbeta) of the T cell receptor (TcR). This interaction triggers the activation (proliferation) of the targeted T lymphocytes and leads to the in vivo or in vitro release of high amounts of various cytokines and other effectors by immune cells. Each SAg interacts specifically with a characteristic set of Vbeta motifs. The review summarizes our current knowledge on S. **aureus** and S. pyogenes superantigen proteins. The repertoire of the staphylococcal and streptococcal SAgs comprises 24 and 8 proteins, respectively. The staphylococcal SAgs include (i) the classical enterotoxins A, B, C (and antigenic variants), D, E, and the recently discovered enterotoxins G to Q, (ii) **toxic shock** syndrome toxin-1, (iii) exfoliatins A and B. The streptococcal SAgs include the classical pyrogenic exotoxins A and C and the newly identified pyrogenic toxins, G, H, I, J, SMEZ, and SSA. The structural and genomic aspects of these toxins and their molecular relatedness are described as well as the available 3-D crystal structure of some of them and that of certain of their complexes with **MHC class II** molecules and the TcR, respectively. The pathophysiological properties and clinical disorders related to these SAgs are reviewed.

3/3,AB/4 (Item 4 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

15182024 Document Delivery Available: 000179489000010 References: 41
TITLE: Epitope mapping of neutralizing TSST-1 specific antibodies induced by immunization with toxin or toxoids
AUTHOR(S): Gampfer JM (REPRINT); Samstag A; Waclavicek M; Wolf HM; Eibl MM; Gulle H
AUTHOR(S) E-MAIL: joerg.gampfer@biomed-research.at
CORPORATE SOURCE: Biomed Forsch Gesell mbH, Schwarzspanierstr 15-1-19/A-1090 Vienna//Austria/ (REPRINT); Biomed Forsch Gesell mbH, /A-1090 Vienna//Austria/; Immunol Tagesklin, /A-1090 Vienna//Austria/
PUBLICATION TYPE: JOURNAL
PUBLICATION: VACCINE, 2002, V20, N31-32 (NOV 1), P3675-3684
GENUINE ARTICLE#: 619RA
PUBLISHER: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
ISSN: 0264-410X
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: **Toxic shock** syndrome toxin-1 (TSST-1), a superantigen produced by Staphylococcus aureus, is a potent stimulator of the immune system. T-cells are activated by crosslinking of **MHC class II** molecules on antigen presenting cells with T-cell receptors (TCR). TSST-I is associated with the majority of the cases of menstrual staphylococcal **toxic shock**, a severe and life-threatening multisystem disorder. Even though antibody mediated protection has been studied, information on antibody specificity directed to individual antigenic determinants of the protein is incomplete.

To obtain immunogens with low toxicity, we generated a double-site mutant (dmTSST-1), modified at solvent-exposed residues predicted to be important for both MHC class II and TCR binding, and detoxified recombinantly expressed TSST-1 (rTSST-1) as well as native TSST-1 (nTSST-1) isolated from Staphylococcus **aureus** by treatment with formaldehyde. Rabbits were immunized with rTSST-1, nTSST-1, dmTSST-1, and formaldehyde inactivated toxoids. The sera obtained were used to map the antigen-reactive regions of the molecule and to identify specificities of antibodies induced by immunization with the different antigens. To detect linear antigenic epitopes of TSST-1 the reactivity of the sera with 11-meric peptides having an overhang of four residues, covering the entire molecule of TSST-1, have been studied. We found that sera of TSST-1 immunized rabbits predominantly reacted with N-terminal residues 1-15, while sera generated with formaldehyde inactivated toxoid recognized a total of 7 regions located at the N- and C-terminus and internal sites of TSST-1. Despite different specificities all sera were able to inhibit TSST-1 induced proliferation of human mononuclear cells. (C) 2002 Elsevier Science Ltd. All rights reserved.

3/3,AB/5 (Item 5 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

15107265 Document Delivery Available: 000179375200021 References: 60
TITLE: Characterization of a novel staphylococcal enterotoxin-like superantigen, a member of the group V subfamily of pyrogenic toxins
AUTHOR(S): Orwin PM; Leung DYM; Tripp TJ; Bohach GA; Earhart CA; Ohlendorf DH; Schlievert PM (REPRINT)

AUTHOR(S) E-MAIL: pats@lenti.med.umn.edu
CORPORATE SOURCE: Univ Minnesota, Dept Microbiol, 420 Delaware St SE/Minneapolis//MN/55455 (REPRINT); Univ Minnesota, Dept Microbiol, /Minneapolis//MN/55455; Univ Minnesota, Dept Biochem, /Minneapolis//MN/55455; Natl Jewish Med & Res Ctr, Dept Pediat, /Denver//CO/80206; Univ Idaho, Dept Microbiol Mol Biol & Biochem, /Moscow//ID/83843
PUBLICATION TYPE: JOURNAL
PUBLICATION: BIOCHEMISTRY, 2002, V41, N47 (NOV 26), P14033-14040
GENUINE ARTICLE#: 617RT
PUBLISHER: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA
ISSN: 0006-2960
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Staphylococcus aureus is an important human pathogen, causing a variety of diseases. Major virulence factors of this organism include staphylococcal enterotoxins (SEs) that cause food poisoning and **toxic shock** syndrome. Our study identified a novel enterotoxin-like protein that is a member of the new subfamily (group V) of pyrogenic toxin superantigens (PTSAgs) and examined its biochemical and immunobiological properties. The gene encoding the SE-like protein is directly 5' of another recently identified PTSAg, SEK. The SE-like protein had a molecular weight of 26000 and an experimentally determined isoelectric point between 7.5 and 8.0. We demonstrated that the PTSAg had many of the biological activities associated with SEs, including superantigenicity, pyrogenicity, and ability to enhance endotoxin shock, but lacked both lethality in rabbits when administered in subcutaneous miniosmotic pumps and emetic activity in monkeys. Recombinant protein stimulated human CD4 and CD8 T cells in a T cell receptor variable region, beta chain (TCRVbeta) specific manner. T cells bearing TCRVbeta 2, 5.1, and 21.3 were significantly stimulated.

3/3,AB/6 (Item 6 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

13203346 References: 12
TITLE: Use of intravenous immunoglobulin in the treatment of staphylococcal and streptococcal **toxic shock** syndromes and related illnesses
AUTHOR(S): Schlievert PM (REPRINT)
CORPORATE SOURCE: Univ Minnesota, Dept Microbiol, 410 Delaware St SE/Minneapolis//MN/55455 (REPRINT); Univ Minnesota, Dept Microbiol, /Minneapolis//MN/55455
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, 2001, V108, N4,S (OCT), PS107-S110
GENUINE ARTICLE#: 487KL
PUBLISHER: MOSBY, INC, 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318 USA
ISSN: 0091-6749
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Pyrogenic toxin superantigens comprise a large family of exotoxins made by Staphylococcus aureus and group A streptococci. These toxins include **toxic shock** syndrome toxin-1, the staphylococcal

enterotoxins, and the streptococcal pyrogenic exotoxins (synonyms: scarlet fever toxins and erythrogenic toxins), all of which have the ability to cause **toxic shock** syndromes and related illnesses. These toxins have a similar three-dimensional structure that allows them to interact with relatively invariant regions of **major histocompatibility complex class II** molecules on the surface of antigen-presenting cells and with certain variable regions of the T-cell receptor-beta chain. The consequence of these interactions (and other immunobiological properties of the toxins) is the exaggerated release of bioactive cytokines. The latter molecules are responsible for the clinical signs of illness associated with these toxins.

3/3,AB/7 (Item 7 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

13175967 References: 179
TITLE: **Toxic shock** syndrome and bacterial superantigens: An update
AUTHOR(S): McCormick JK (REPRINT); Yarwood JM; Schlievert PM
AUTHOR(S) E-MAIL: jmccormi@lenti.med.umn.edu; yarwood@lenti.med.umn.edu; pats@lenti.med.umn.edu
CORPORATE SOURCE: Univ Minnesota, Dept Microbiol, /Minneapolis//MN/55455 (REPRINT); Univ Minnesota, Dept Microbiol, /Minneapolis//MN/55455
PUBLICATION TYPE: JOURNAL
PUBLICATION: ANNUAL REVIEW OF MICROBIOLOGY, 2001, V55, P77-104
GENUINE ARTICLE#: 485BA
PUBLISHER: ANNUAL REVIEWS, 4139 EL CAMINO WAY, PO BOX 10139, PALO ALTO, CA 94303-0139 USA
ISSN: 0066-4227
LANGUAGE: English DOCUMENT TYPE: REVIEW

ABSTRACT: **Toxic shock** syndrome (**TSS**) is an acute onset illness characterized by fever, rash formation, and hypotension that can lead to multiple organ failure and lethal shock, as well as desquamation in patients that recover. The disease is caused by bacterial superantigens (SAGs) secreted from Staphylococcus aureus and group A streptococci. SAGs bypass normal antigen presentation by binding to **class II major histocompatibility complex** molecules on antigen-presenting cells and to specific variable regions on the beta -chain of the T-cell antigen receptor. Through this interaction, SAGs activate T cells at orders of magnitude above antigen-specific activation, resulting in massive cytokine release that is believed to be responsible for the most severe features of **TSS**. This review focuses on clinical and epidemiological aspects of **TSS**, as well as important developments in the genetics, biochemistry, immunology, and structural biology of SAGs. From the evolutionary relationships between these important toxins, we propose that there are five distinct groups of SAGs.

3/3,AB/8 (Item 8 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

12274853 References: 57

TITLE: Structural evidence for the evolution of pyrogenic toxin superantigens
AUTHOR(S): Mitchell DT; Levitt DG; Schlievert PM; Ohlendorf DH (REPRINT)
CORPORATE SOURCE: Univ Minnesota, Dept Biochem, 6-155 Jackson Hall,321 Church St SE/Minneapolis//MN/55455 (REPRINT); Univ Minnesota, Dept Biochem, /Minneapolis//MN/55455; Univ Minnesota, Dept Physiol, /Minneapolis//MN/55455; Univ Minnesota, Dept Microbiol, /Minneapolis//MN/55455
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF MOLECULAR EVOLUTION, 2000, V51, N6 (DEC), P520-531
GENUINE ARTICLE#: 385PQ
PUBLISHER: SPRINGER-VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010 USA
ISSN: 0022-2844
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Pathogenic bacteria have evolved a wide variety of toxins to invade and attack host organisms. In particular, strains of the bacteria Staphylococcus aureus and Streptococcus pyogenes produce a family of pyrogenic toxin superantigens (PTSAgs) that can cause illness, e.g., **toxic shock** syndrome, or synergize with a number of other immune system disorders. The PTSAgs are all similar in size and have a conserved two-domain tertiary fold despite minimal amino acid sequence identity. The tertiary structure of PTSAg domain 1 is similar to the immunoglobulin binding motif of streptococcal proteins G and L. PTSAg domain 2 resembles members of the oligosaccharide/oligonucleotide binding fold family that includes the B subunits of the AB(5) heat-labile enterotoxins, cholera toxin, pertussis toxin, and verotoxin. The strong structural homology between the pyrogenic toxins and other bacterial proteins suggests that the PTSAgs evolved through the recombination of two smaller beta -strand motifs.

3/3,AB/9 (Item 9 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

11407861 References: 51
TITLE: Superantigens - powerful modifiers of the immune system
AUTHOR(S): Fraser J (REPRINT); Arcus V; Kong P; Baker E; Proft T
AUTHOR(S) E-MAIL: j.d.fraser@auckland.ac.nz
CORPORATE SOURCE: Univ Auckland, Dept Mol Med, Private Bag 92019/Auckland//New Zealand/ (REPRINT); Univ Auckland, Dept Mol Med, /Auckland//New Zealand/
PUBLICATION TYPE: JOURNAL
PUBLICATION: MOLECULAR MEDICINE TODAY, 2000, V6, N3 (MAR), P125-132
GENUINE ARTICLE#: 290LX
PUBLISHER: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
ISSN: 1357-4310
LANGUAGE: English DOCUMENT TYPE: REVIEW

ABSTRACT: Superantigens are powerful microbial toxins that activate the immune system by binding to class II major histocompatibility complex and T-cell receptor molecules. They cause a number of diseases characterized by fever and shock and are important virulence factors for two human commensal organisms, Staphylococcus **aureus** and Streptococcus pyogenes, as well

as for some viruses. Their mode of action and variation around the common theme of over-stimulating T cells, provides a rich insight into the constant battle between microbes and the immune system.

3/3,AB/10 (Item 10 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

11074259 References: 15
TITLE: The effect of site-specific monoclonal antibodies directed to **toxic shock** syndrome toxin-1 in experimental Staphylococcus aureus arthritis
AUTHOR(S): Verdrengh M (REPRINT); Kum W; Chow A; Tarkowski A
AUTHOR(S) E-MAIL: margareta.verdrengh@immuno.gu.se
CORPORATE SOURCE: Gothenburg Univ, Dept Rheumatol, Guldhedsgatan 10A/S-41346 Gothenburg//Sweden/ (REPRINT); Gothenburg Univ, Dept Rheumatol, /S-41346 Gothenburg//Sweden/; Univ British Columbia, Dept Med, /Vancouver/BC V5Z 1M9/Canada/
PUBLICATION TYPE: JOURNAL
PUBLICATION: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, 1999, V118, N2 (NOV), P 268-270
GENUINE ARTICLE#: 253CL
PUBLISHER: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND
ISSN: 0009-9104
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Staphylococcus aureus produces a large number of potential virulence factors, among these the superantigen **toxic shock** syndrome toxin-1 (TSST-1). We have recently demonstrated that TSST-1 is involved in the pathogenesis of septic arthritis. Recent data show that the TSST-1 molecule is composed of two distinct domains, one proposed to interact with T cell receptor (TCR) and one with the **MHC class II**. The aim of this study was to assess if interaction between TSST-1-specific MoAbs directed to sites on the MHC and/or TCR V beta affects the development of experimental S. **aureus**-induced arthritis. For that purpose we used a panel of seven MoAbs, which were injected intraperitoneally before and after inoculation with a TSST-1-producing S. **aureus** strain. Administration of antibodies did not affect the development of arthritis, suggesting inefficacy of such a procedure in neutralization of exotoxin-mediated disease manifestations.

3/3,AB/11 (Item 11 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

09683037 References: 40
TITLE: Roxithromycin down-modulates antigen-presenting and interleukin-1 beta-producing abilities of murine Langerhans cells
AUTHOR(S): Ohshima A (REPRINT); Tokura Y; Wakita H; Furukawa F; Takigawa M
CORPORATE SOURCE: HAMAMATSU UNIV,SCH MED, DEPT DERMATOL, 3600 HANDA CHO/HAMAMATSU/SHIZUOKA 4313192/JAPAN/ (REPRINT)
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF DERMATOLOGICAL SCIENCE, 1998, V17, N3 (JUL), P

214-222
GENUINE ARTICLE#: 103EF
PUBLISHER: ELSEVIER SCI IRELAND LTD, CUSTOMER RELATIONS MANAGER, BAY 15, SHANNON INDUSTRIAL ESTATE CO, CLARE, IRELAND
ISSN: 0923-1811
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The immunomodulatory effect of the macrolide antibiotic, roxithromycin (RXM) on Langerhans cells (LC) was studied in mice. RXM inhibited the ability of LC to present superantigen and hapten to T cells at 100 mu M. The superantigen-presenting activity of LC was more profoundly abrogated by RXM than the hapten-presenting activity. This functional reduction was partly attributed to an RXM-induced decrease in promotion of the expression of major histocompatibility complex class II molecules on LC. On the other hand, RXM down-modulated the production of interleukin-1 beta by LC at a lower concentration of 10 mu M than concentrations that inhibited antigen presentation. These results imply that RXM exerts therapeutic effectiveness via not only bacteriocidal action but also inhibitory effect on the LC ability in **T-cell**-mediated cutaneous **diseases** that can be exacerbated by skin-colonized Staphylococcus **aureus**.

3/3,AB/12 (Item 12 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

09499444 References: 23
TITLE: V beta 11(+) T-lymphocyte expansion by **toxic shock** syndrome toxin-1 differs in mice bearing H-2(q) versus H-2(b) haplotypes
AUTHOR(S): Zhao YX (REPRINT); Brunsberg U; Holmdahl R; Tarkowski A
CORPORATE SOURCE: TORONTO HOSP,ARTHRIT CTR, 13-415 MC, 399 BATHURST ST/TORONTO/ON M5T 2S8/CANADA/ (REPRINT); UNIV GOTHENBURG,DEPT RHEUMATOL/GOTHENBURG//SWEDEN/; UNIV GOTEBORG,DEPT CLIN IMMUNOL/GOTHENBURG//SWEDEN/; LUND UNIV,DEPT MED INFLAMMAT RES/S-22100 LUND//SWEDEN/
PUBLICATION TYPE: JOURNAL
PUBLICATION: IMMUNOLOGY, 1998, V94, N1 (MAY), P1-4
GENUINE ARTICLE#: ZP705
PUBLISHER: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND
ISSN: 0019-2805
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: We have recently demonstrated that **toxic shock** syndrome toxin-1 (TSST-1) expanded V beta 11(+) T lymphocytes contribute to Staphylococcus aureus arthritis and sepsis-induced mortality. Interestingly, V beta 11(+) T-cell mediated joint pathology varies in different mouse strains. In this study, we characterized the in vitro pattern of V beta 11(+) T-cell expansion by TSST-1 in mice with various genetic backgrounds. Mice expressing **major histocompatibility complex (MHC) class II** I-E molecules did not expand V beta 11(+) T cells upon stimulation with TSST-1. Using B10 congeneic I-E negative mouse strains, we found that the TSST-1-expanded V beta 11(+) T

cells in B10Q (H-2(q)) and B10M (H-2(f)) mice but not in B10B (H-2(b)) mice. Antigen-presenting cells (APC) from B10Q mice, L cells and lymphoma cell line transfected with a q gene did not restore the deficient V beta 11(+) T-cell expansion by TSST-1 in purified T cells from B10B mice. In contrast, I-A(b) APC were able to stimulate V beta 11(+) T cells from H-2(q) mice. Furthermore, V beta 11(+) T cells in H-2(b) mice did expand when exposed to staphylococcal enterotoxin A (SEA). These findings suggest that the T-cell repertoire, skewed by clonal deletion and inactivation of self-reactive T cells, accounts for the different magnitude of V beta 11(+) T-cell expansion among the different mouse strains.

3/3,AB/13 (Item 13 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

08586620 References: 31
TITLE: Selective binding of bacterial toxins to major histocompatibility complex class II-expressing cells is controlled by invariant chain and HLA-DM
AUTHOR(S): Lavoie PM; Thibodeau J; Cloutier I; Busch R; Sekaly RP (REPRINT)
CORPORATE SOURCE: INST RECH CLIN MONTREAL,IMMUNOL LAB, 110 AVE PINS OUEST/MONTREAL/PQ H2W 1R7/CANADA/ (REPRINT); INST RECH CLIN MONTREAL,IMMUNOL LAB/MONTREAL/PQ H2W 1R7/CANADA/; MCGILL UNIV,SCH MED, DEPT EXPT MED/MONTREAL/PQ H3A 1A3/CANADA/; INST PASTEUR,UNITE IMMUNOCHIM ANALYT/F-75724 PARIS 15//FRANCE/; STANFORD UNIV,MED CTR, DEPT PEDIAT/STANFORD//CA/94305
PUBLICATION TYPE: JOURNAL
PUBLICATION: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, 1997, V94, N13 (JUN 24), P6892-6897
GENUINE ARTICLE#: XH034
PUBLISHER: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON, DC 20418
ISSN: 0027-8424
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Bacterial superantigens (Sr-fgs) bind to major histocompatibility complex (MHC) class II molecules and activate T cells in a V beta-restricted fashion. We recently identified subsets of HLA-DR1 molecules that show selectivity for SAgs. Here, we extend these observations Sv showing that different cell lineages demonstrate distinct SAg-binding specificities although they: all express HLA-DR1. Indeed, If cells bind staphylococcal enterotoxin A (SEA) and **toxic shock** syndrome toxin 1 (TSST-1) with high affinity while staphylococcal enterotoxin B (SEE) binding is barely detectable, In contrast, DR1-transfected HeLa cells show efficient binding of SEE, but not of SEA or TSST-1. We investigated the class II maturation events required for efficient interaction with SAgs and found that the ability of cells to bind and present the toxins can be drastically modulated by coexpression of the class II-associated invariant chain (Ii) and HLA-DM. SEA binding to DBI molecules required coexpression of Ii, whereas TSST-1 binding was selectively enhanced by RI, Binding of SEE was affected by cell type-specific factors other than Ii or DM. The selectivity of SAgs for different MNC class II populations was minimally affected by HLA-DR intrinsic polymorphism and could not be explained by binding to alternative sites on DR molecules, Our results indicate that SAgs are sensitive to

structural heterogeneity in class II molecules, which is consequent to the differential regulation of expression of antigen processing cofactors. Therefore, me speculate that Staphylococcus **aureus** have retained the ability to express numerous SAgs in adaptation to the microheterogeneity displayed by **MHC class II** molecules and that this may relate to their ability to infect different tissues.

3/3,AB/14 (Item 14 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

08399327 References: 50
TITLE: Transcytosis of staphylococcal superantigen toxins
AUTHOR(S): Hamad ARA; Marrack P; Kappler JW (REPRINT)
CORPORATE SOURCE: NATL JEWISH CTR IMMUNOL & RESP MED,DEPT MED, DIV BASIC IMMUNOL, 1400 JACKSON ST/DENVER//CO/80206 (REPRINT); NATL JEWISH CTR IMMUNOL & RESP MED,DEPT MED, DIV BASIC IMMUNOL/DENVER//CO/80206; UNIV COLORADO,HLTH SCI CTR, DEPT BIOCHEM BIOPHYS & GENET/DENVER//CO/80262; UNIV COLORADO,HLTH SCI CTR, DEPT IMMUNOL/DENVER//CO/80262; UNIV COLORADO,HLTH SCI CTR, DEPT MED/DENVER//CO/80262
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF EXPERIMENTAL MEDICINE, 1997, V185, N8 (APR 21), P 1447-1454
GENUINE ARTICLE#: WW047
PUBLISHER: ROCKEFELLER UNIV PRESS, 1114 FIRST AVE, 4TH FL, NEW YORK, NY 10021
ISSN: 0022-1007
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Staphylococcus aureus produces a set of proteins (e.g., staphylococcal enterotoxin A [SEA], SEB, **toxic shock** syndrome toxin 1 [TSST-1]) which act both as superantigens (SAgs) and toxins. Although their mode of action as SAgs is well understood, little is known about how they enter the body via the intestine and cause food poisoning. To examine this problem we used an in vitro culture system to study the capacity of **class II MHC**-negative human intestinal epithelial cells (Caco-2) to transcytose several staphylococcal toxins. We found that Caco-2 cells are capable of dose-dependent, facilitated transcytosis of SEB and TSST-1, but not SEA. We extended these studies in vivo in mice by showing that ingested SEB appears in the blood more efficiently than SEA. Our data suggest that these toxins can cross the epithelium in an immunologically intact form. These results may have important implications for the pathogenesis of food poisoning.

3/3,AB/15 (Item 15 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

08281470 References: 28
TITLE: Major histocompatibility complex class II region confers susceptibility to Staphylococcus **aureus** arthritis
AUTHOR(S): Abdelnour A; Zhao YX; Holmdahl R; Tarkowski A (REPRINT)
CORPORATE SOURCE: GOTHENBURG UNIV,DEPT RHEUMATOL, GULDHESGATAN 10/S-41346 GOTHENBURG//SWEDEN/ (REPRINT); GOTHENBURG UNIV,DEPT RHEUMATOL/S-41346

GOTHENBURG//SWEDEN/; GOTHENBURG UNIV,DEPT CLIN IMMUNOL/S-41346
GOTHENBURG//SWEDEN/; LUND UNIV,DEPT MED INFLAMAT/LUND//SWEDEN/
PUBLICATION TYPE: JOURNAL
PUBLICATION: SCANDINAVIAN JOURNAL OF IMMUNOLOGY, 1997, V45, N3 (MAR), P 301-307
GENUINE ARTICLE#: WN234
PUBLISHER: BLACKWELL SCIENCE LTD, OSNEY MEAD, OXFORD, OXON, ENGLAND OX2 0EL
ISSN: 0300-9475
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The importance of the MHC class II region for the development of septic arthritis was studied in a murine model of haematogenously induced Staphylococcus **aureus** arthritis. In the first experiment **MHC class II** deficient mice (A beta(-/-)) and their heterozygous (A beta(+/-)) littermates were intravenously inoculated with a single dose of **toxic shock** syndrome toxin-1 producing S. **aureus** LS-1 strain. The results demonstrate that the expression of **class II MHC** molecules increases the prevalence and severity of arthritis. To analyse the impact of **MHC class II** haplotypes on the disease onset and progression the authors used congenic C3H.NB, C3H.Q and C3H/HeJ mice in the second set of experiments. The results show that C3H/HeJ mice developed the highest frequency and the most severe course of arthritis compared with C3H.NB and C3H.Q animals. Immunohistochemical analysis of arthritic joints revealed equal number of macrophages, CD4(+) and CD8(+) lymphocytes in the inflamed synovia in all the congenic mice. In contrast, the number of **MHC class II** expressing cells was higher in the arthritic joints of C3H/HeJ mice compared with the congenic strains ($P < 0.001$). Furthermore, serum levels of proarthrtitogenic cytokines, such as tumour necrosis factor and interleukin-6 were higher in C3H/HeJ group. This study indicates that **MHC class II** expression is necessary for the development of S. **aureus** arthritis in mice and that different **MHC class II** haplotypes confer varying susceptibility for development of joint inflammation induced by staphylococci.

3/3,AB/16 (Item 16 from file: 440)

08223521 References: 65
TITLE: MHC class II-dependent abnormal reactivity toward bacterial superantigens in immune cells of NOD mice
AUTHOR(S): Radons J (REPRINT); Burkart V; Kolb H
CORPORATE SOURCE: UNIV DUSSELDORF,DIABET RES INST, HENNEKAMP 65/D-40225 DUSSELDORF//GERMANY/ (REPRINT)
PUBLICATION TYPE: JOURNAL
PUBLICATION: DIABETES, 1997, V46, N3 (MAR), P379-385
GENUINE ARTICLE#: WK107
PUBLISHER: AMER DIABETES ASSOC, 1660 DUKE ST, ALEXANDRIA, VA 22314
ISSN: 0012-1797
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Superantigens have been implicated in the pathogenesis of type I diabetes and other immune-mediated diseases. We therefore tested the hypothesis of an abnormal reactivity of the immune system toward bacterial

superantigens during the prediabetic phase. For this purpose, splenocytes from NOD (H-2(g7)) mice were exposed to two well-characterized superantigens: Staphylococcal aureus enterotoxin-B (SEB) and **toxic shock** syndrome toxin-1 (TSST-1). Cells from BALB/c (H-2(d)) and C57BL/6 (H-2(b)) mice as well as those from NON (H-2(non)) and NOR (H-2(g7)) mice were used as controls. After 72 h of co-culture with the superantigens or the mitogen concanavalin A (Con A), proliferative response and mitochondrial activity were determined. In the culture supernatants, the cytokines gamma-interferon (IFN-gamma) and interleukin 10 (IL-10) were measured. Striking similarities between NOD cells and major histocompatiblity complex (MHC)-identical NOR cells could be observed with regard to a low proliferative and mitochondrial response to SEB, accompanied by a normal response to TSST-1 and Con A, respectively. In addition, only NOD and NOR spleen cells were low producers of the T-helper 1 (Th1) cytokine IFN-gamma in response to SEB. Conversely, abnormally high IFN-gamma levels were induced by TSST-1 in NOD and NOR spleen cells. The cytokine response to Con A was also biased toward IFN-gamma in both NOD and NOR. Since IFN-gamma and IL-10 are crucial disease-promoting or -protecting mediators in prediabetic NOD mice, superantigens may affect pathogenesis by acting on the Th1/Th2 cytokine balance. The low responder status toward SEB in NOD spleen cells may be of pathogenetic relevance in view of recent findings that the insulin B-chain also interacts with the SEB binding site on **MHC class II** molecules. In conclusion, we show here that immune cells from mice with a diabetes-associated MHC type respond differently to common environmental superantigens than do immune cells from control strains.

3/3,AB/17 (Item 17 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

07639974 References: 121
TITLE: SUPERANTIGEN AS A MODIFYING FACTOR IN HIV INFECTION
AUTHOR(S): KOBAYASHI N; URASAWA S
CORPORATE SOURCE: SAPPORO MED UNIV,SCH MED,DEPT HYG,CHUO KU,S-1,W-17/SAPPORO/HOKKAIDO 060/JAPAN/ (Reprint)
PUBLICATION: PEDIATRIC AIDS AND HIV INFECTION-FETUS TO ADOLESCENT, 1996, V7, N3 (JUN), P143-154
GENUINE ARTICLE#: VB604
ISSN: 1045-5418
LANGUAGE: ENGLISH DOCUMENT TYPE: REVIEW

ABSTRACT: Superantigen is characterized as a potent stimulator of T cells through its unique interaction with major histocompatibility complex class II molecule and the V-<beta> chain of T cell receptor. It has been reported that. symptoms in several infectious diseases are associated with superantigen activity, i.e., abnormal reaction due to excess activation of T cells. However, the implications of superantigen in human immunodeficiency virus (HIV) infections have not been well elucidated. In this article, we review the possible mechanisms by which superantigens may modify HIV infections. In conclusion, superantigen is considered to be a factor that aggravates the immunodeficient state in HIV-infected patients through activation of HIV expression in infected T cells and monocytes, and facilitation of CD4 T cell depletion. Since exogenous superantigen is most likely to be provided by microbial infections such as Staphylococcus

aureus infection, countermeasures against these complicating infections may be important to avert the detrimental impact of superantigens.

3/3,AB/18 (Item 18 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

06671939 References: 79
TITLE: CRYSTAL STRUCTURE OF THE SUPERANTIGEN ENTEROTOXIN C2 FROM STAPHYLOCOCCUS AUREUS REVEALS A ZINC-BINDING SITE
AUTHOR(S): PAPAGEORGIOU AC; ACHARYA KR (Reprint); SHAPIRO R; PASSALACQUA EF ; BREHM RD; TRANTER HS
CORPORATE SOURCE: UNIV BATH,SCH BIOL & BIOCHEM/BATH BA2 7AY/AVON/ENGLAND/ (Reprint); UNIV BATH,SCH BIOL & BIOCHEM/BATH BA2 7AY/AVON/ENGLAND/; HARVARD UNIV,SCH MED,CTR BIOCHEM & BIOPHYS SCI & MED/BOSTON//MA/02115; HARVARD UNIV,SCH MED,DEPT PATHOL/BOSTON//MA/02115; PUBL HLTH LAB SERV,CTR APPL MICROBIOL & RES,DEPT DEV PROD/SALISBURY SP4 0JG/WILTS/ENGLAND/
PUBLICATION: STRUCTURE, 1995, V3, N8 (AUG 15), P769-779
GENUINE ARTICLE#: RP892
ISSN: 0969-2126
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Background: Staphylococcus aureus enterotoxin C2 (SEC2) belongs to a family' of proteins, termed 'superantigens', that form complexes with **class II MHC** molecules enabling them to activate a substantial number of T cells. Although superantigens seem to act by a common mechanism, they vary in many of their specific interactions and biological properties. Comparison of the structure of SEC2 with those of two other superantigens - staphylococcal enterotoxin B (SEE) and **toxic shock** syndrome toxin-1 (TSST-1) - may provide insight into their mode of action.

Results: The crystal structure of SEC2 has been determined at 2.0 Angstrom resolution. The overall topology of the molecule resembles that of SEE and TSST-1, and the regions corresponding to the MHC class II and T-cell receptor binding sites on SEE are quite similar in SEC2. A unique feature of SEC2 is the presence of a zinc ion located in a solvent-exposed region at the interface between the two domains of the molecule. The zinc ion is coordinated to Asp83, His118, His122 and Asp9* (from the neighbouring molecule in the crystal lattice). Atomic absorption spectrometry demonstrates that zinc is also bound to SEC2 in solution.

Conclusions: SEC2 appears to be capable of binding to MHC class II molecules in much the same manner as SEE. However, structure-function studies have suggested an alternative binding mode that involves a different site on the toxin. The zinc ion of SEC2 lies within this region and thus may be important for complex formation, for example by acting as a bridge between the two molecules. Other possible roles for the metal cation, including a catalytic one, are also considered.

3/3,AB/19 (Item 19 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

06580450 References: 31
TITLE: SUPERANTIGENS - DO THEY HAVE A ROLE IN SKIN DISEASES
AUTHOR(S): SKOV L; BAADSGAARD O (Reprint)
CORPORATE SOURCE: UNIV COPENHAGEN,GENTOFTE HOSP,DEPT DERMATOL,NIELS ANDERSENS VEJ 65/DK-2900 HELLERUP//DENMARK/ (Reprint); UNIV COPENHAGEN,GENTOFTE HOSP,DEPT DERMATOL/DK-2900 HELLERUP//DENMARK/
PUBLICATION: ARCHIVES OF DERMATOLOGY, 1995, V131, N7 (JUL), P829-832
GENUINE ARTICLE#: RH814
ISSN: 0003-987X
LANGUAGE: ENGLISH DOCUMENT TYPE: REVIEW

ABSTRACT: Superantigens are a group of bacterial and viral proteins that are characterized by their capacity to stimulate a large number of T cells. They bind directly to the major histocompatibility complex class II molecule on the antigen-presenting cell and cross-link the antigen-presenting cell with T cells expressing certain T-cell receptors, leading to polyclonal T-cell activation. They have been shown to play a role in **toxic shock** syndrome and mucocutaneous lymph node syndrome and are postulated to play a role in other systemic diseases. Because inflammatory skin diseases such as atopic dermatitis and psoriasis are often known to be colonized with superantigen-releasing Staphylococcus **aureus**, the role of superantigens in skin diseases is of major importance. Recent studies have demonstrated that if a staphylococcal superantigen is applied on intact human skin, a clinical picture of dermatitis evolves. Furthermore, in the presence of superantigens, epidermal cells potently activate T cells. Thus, superantigens may play a role in the induction and exacerbation of inflammatory skin diseases.

3/3,AB/20 (Item 20 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

06445281 References: 37
TITLE: A **TOXIC SHOCK** SYNDROME TOXIN 1 MUTANT THAT DEFINES FUNCTIONAL SITE CRITICAL FOR T-CELL ACTIVATION
AUTHOR(S): CULLEN CM; BLANCO LR; BONVENTRE PF; CHOI E (Reprint)
CORPORATE SOURCE: UNIV CINCINNATI,COLL MED,DEPT MOLEC GENET BIOCHEM & MICROBIOL,231 BETHESDA AVE,ML 524/CINCINNATI//OH/45267 (Reprint); UNIV CINCINNATI,COLL MED,DEPT MOLEC GENET BIOCHEM & MICROBIOL/CINCINNATI//OH/45267
PUBLICATION: INFECTION AND IMMUNITY, 1995, V63, N6 (JUN), P2141-2146
GENUINE ARTICLE#: RA191
ISSN: 0019-9567
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: **Toxic shock** syndrome toxin 1 (TSST-1), a superantigen produced by Staphylococcus aureus, is a causative agent of **toxic shock** syndrome (**TSS**). This superantigen is a potent stimulator of T cells and macrophages/monocytes, resulting in the release of cytokines that are implicated in the pathogenesis of **TSS**. This study characterizes a mutant TSST-1, derived by site-directed mutagenesis, that has an alanine substitution at histidine 135 (mutant 135). This single-amino-acid change results in a mutant toxin that has lost mitogenic activity for T cells. In contrast to wild-type TSST-1, this mutant does not

induce T cells to express interleukin-2, gamma interferon, or tumor necrosis factor beta (TNF-beta). The inability of mutant 135 to activate T cells is not due to a lack of binding to the **class II major histocompatibility complex** receptor. In addition, the mutant TSST-1 does not induce expression of TNF-alpha, which plays a role in the development of lethal shock. The lack of TNF-alpha induction by mutant 135 is likely due to its inability to activate T cells. These data suggest that the mutation at histidine 135 in TSST-1 affects toxin interactions with the T-cell receptor rather than the **class II major histocompatibility complex** receptor.

3/3,AB/21 (Item 21 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

06440071 References: 67
TITLE: SEQUENCE ANALYSIS OF THE GENE FOR A NOVEL SUPERANTIGEN PRODUCED BY YERSINIA PSEUDOTUBERCULOSIS AND EXPRESSION OF THE RECOMBINANT PROTEIN
AUTHOR(S): ITO Y; ABE J; YOSHINO K; TAKEDA T; KOHSAKA T
CORPORATE SOURCE: NATL CHILDRENS MED RES CTR,DEPT ALLERGY & IMMUNOL,SETAGAYA KU,3-35-31 TAISHIDO/TOKYO 154//JAPAN/ (Reprint); NATL CHILDRENS MED RES CTR,DEPT INFECT DIS RES,SETAGAYA KU/TOKYO 154//JAPAN/
PUBLICATION: JOURNAL OF IMMUNOLOGY, 1995, V154, N11 (JUN 1), P5896-5906
GENUINE ARTICLE#: RB197
ISSN: 0022-1767
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: We previously reported that the Gram-negative bacterium Yersinia pseudotuberculosis produces a superantigen (YPM, Y. pseudotuberculosis-derived mitogen) that expands T cells bearing V beta s 3, 9, 13.1, and 13.2 in an MHC class II-dependent manner. Based on the previously determined N-terminal 23 amino acids of YPM (T-D-Y-D-N-T-L-N-S-I-P-S-L-R-I-P-N-I-A-T-Y-T-G- (one-letter code)), we cloned the ypm gene and analyzed the nucleotide sequence. The gene encodes a 151-amino acid protein with a 20-amino acid signal peptide at its N terminus. The recombinant YPM expressed by the cloned gene exerted a mitogenic activity on human PBMC at a concentration of approximately 1 pg/ml. T cells bearing V beta 13.3 were preferentially expanded as well as T cells bearing the same V beta repertoires stimulated by native YPM. T cells were stimulated by the recombinant YPM in the presence of either fixed or unfixed HLA class II-transfected mouse fibroblasts. Furthermore, sequence diversity in the junctional region of the TCR beta-chain containing the V beta 3 element could be observed after stimulation by the recombinant YPM. These results indicate that YPM belongs to the category of superantigens and should be included as a novel member. The amino acid sequence of the mature protein showed no significant homology to other superantigens derived from Gram-positive bacteria such as Staphylococcus **aureus** and Streptococcus pyogenes. This observation, together with the substantially smaller m.w. suggest that ypm must have evolved from a different ancestral gene.

3/3,AB/22 (Item 22 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

06377001 References: 33
TITLE: PROLIFERATIVE RESPONSE AND CYTOKINE PRODUCTION OF BOVINE PERIPHERAL BLOOD MONONUCLEAR CELLS INDUCED BY THE SUPERANTIGENS STAPHYLOCOCCAL ENTEROTOXINS AND **TOXIC SHOCK** SYNDROME TOXIN-1
AUTHOR(S): YOKOMIZO Y; MORI Y; SHIMOJI Y; SHIMIZU S; SENTSUI H; KODAMA M; IGARASHI H
CORPORATE SOURCE: NATL INST ANIM HLTH,3-1-1 KANNONDAI/TSUKUBA/IBARAKI 305/JAPAN/ (Reprint); NATL INST ANIM HLTH,HOKKAIDO BRANCH,TOYOHIRA KU/SAPPORO/HOKKAIDO 062/JAPAN/; TOKYO METROPOLITAN RES LAB PUBL HLTH,SHINJUKU KU/TOKYO 160//JAPAN/
PUBLICATION: JOURNAL OF VETERINARY MEDICAL SCIENCE, 1995, V57, N2 (APR), P 299-305
GENUINE ARTICLE#: QW209
ISSN: 0916-7250
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: The potential of staphylococcal enterotoxin A (SEA), B (SEE), C (SEC) and **toxic shock** syndrome toxin-1 (TSST-1) to act as superantigens by inducing polyclonal T-cell mitogenesis and cytokine production was tested on bovine peripheral blood mononuclear cells (PBMC). These four toxins were capable of inducing strong proliferative response of PBMC from carves over a broad dosage range (1 pg/ml to 1 mu g/ml) in vitro. The toxin-activated blast cells consisted of both CD4(+) T-cells and CD8(+) T-cells, but the T-cell proliferation depended upon the presence of monocytes. Treatment of monocytes with monoclonal antibody to major histocompatibility complex class II antigens substantially inhibited the toxin-induced T-cell proliferative response, but paraformaldehyde-fixation did not abrogate the accessory function. SEA, SEE, SEC and TSST-1, all induced the in vitro release of interleukin-2, interferon gamma and tumor necrosis factor cu in a dose dependent manner. The results indicate that SEA, SEE, SEC and TSST-1 are capable of acting as superantigens by stimulating bovine T-cells as shown in the human and murine systems. The possible implications of these toxins in the immunopathogenesis of bovine mastitis caused by the infection with Staphylococcus **aureus** are discussed.

3/3,AB/23 (Item 23 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

06043464 References: 21
TITLE: MAJOR HISTOCOMPATIBILITY COMPLEX CLASS II BINDING SITE FOR STREPTOCOCCAL PYROGENIC (ERYTHROGENIC) TOXIN A
AUTHOR(S): HARTWIG UF; GERLACH D; FLEISCHER B (Reprint)
CORPORATE SOURCE: BERNHARD NOCHT INST TROP MED,BERNHARD NOCHT STR74/D-20359 HAMBURG//GERMANY/ (Reprint); BERNHARD NOCHT INST TROP MED/D-20359 HAMBURG//GERMANY/; UNIV MAINZ,DEPT MED 1/W-6500 MAINZ//GERMANY/; INST EXPTL MICROBIOL/JENA//GERMANY/
PUBLICATION: MEDICAL MICROBIOLOGY AND IMMUNOLOGY, 1994, V183, N5 (NOV), P 257-264
GENUINE ARTICLE#: PZ780
ISSN: 0300-8584
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Streptococcal pyrogenic exotoxin A (SPEA) is an important pathogenicity factor of group A streptococci. It is a member of the family of ''superantigens'' produced by Staphylococcus aureus and Streptococcus pyogenes and its T lymphocyte stimulating activity is involved into the pathogenesis of certain diseases: caused by pyogenic streptococci. In this study we have produced and characterized recombinant SPEA molecules in Escherichia coli. These molecules are indistinguishable from natural SPEA in both T cell stimulatory and HLA class II binding activities. Human class II molecules are more efficient than mouse class II molecules in presenting SPEA to T cells. In binding tests to **major histocompatibility complex class II**-positive cells SPEA competes with staphylococcal enterotoxin B and A but not with **toxic shock** syndrome toxin-1.

3/3,AB/24 (Item 24 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

05986170 References: 38
TITLE: SUBSETS OF HLA-DR1 MOLECULES DEFINED BY SEB AND TSST-1 BINDING
AUTHOR(S): THIBODEAU J; CLOUTIER I; LAVOIE PM; LABRECQUE N; MOURAD W; JARDETZKY T; SEKALY RP (Reprint)
CORPORATE SOURCE: CLIN RES INST MONTREAL,IMMUNOL LAB,110 PINE AVEW/MONTREAL H2W 1R7/PQ/CANADA/ (Reprint); CLIN RES INST MONTREAL,IMMUNOL LAB/MONTREAL H2W1R7/PQ/CANADA/; UNIV MONTREAL,FAC MED,DEPT IMMUNOL & MICROBIOL/MONTREAL/PQ/CANADA/; MCGILL UNIV,SCH MED,DEPT MICROBIOL & IMMUNOL/MONTREAL H3A 2B4/PQ/CANADA/; CHU LAVAL,DEPT IMMUNOL & RHUMATOL/ST FOY G1V 4G2/PQ/CANADA/; HARVARD UNIV,DEPT BIOCHEM & MOLEC BIOL/CAMBRIDGE//MA/02138
PUBLICATION: SCIENCE, 1994, V266, N5192 (DEC 16), P1874-1878
GENUINE ARTICLE#: PX383
ISSN: 0036-8075
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Superantigens bind to major histocompatibility complex class II molecules on antigen-presenting cells and stimulate T cells. Staphylococcus **aureus** enterotoxin B (SEB) and **toxic shock** syndrome toxin-1 (TSST-1) bind to the same region of human lymphocyte antigen (HL4)-DR1 but do not compete with each other, which indicates that they bind to different subsets of DR1 molecules. Here, a mutation in the peptide-binding groove disrupted the SEB and TSST-1 binding sites, which suggests that peptides can influence the interaction with bacterial toxins. in support of this, the expression of the DR1 molecule in various cell types differentially affected the binding of these toxins.

3/3,AB/25 (Item 25 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

05314850 References: 28
TITLE: CELL ADHESION MOLECULES ARE CO-RECEPTORS FOR STAPHYLOCOCCAL ENTEROTOXIN B-INDUCED T-CELL ACTIVATION AND CYTOKINE PRODUCTION
AUTHOR(S): KRAKAUER T
CORPORATE SOURCE: US ARMY,MED RES INST INFECT DIS,APPL RES DIV,BLDG 1425/FT

DETRICK//MD/21702 (Reprint)
PUBLICATION: IMMUNOLOGY LETTERS, 1994, V39, N2 (FEB), P121-125
GENUINE ARTICLE#: ND852
ISSN: 0165-2478
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Enterotoxins produced by Staphylococcus aureus are potent mitogens for human T cells and cause lethal **toxic shock**. These superantigens bind to **major histocompatibility complex class II** on antigen-presenting cells outside the conventional peptide-binding groove and stimulate T cells expressing certain T-cell receptor V beta gene products. We investigated other cell-surface molecules on human peripheral blood mononuclear cells that can mediate staphylococcal enterotoxin B (SEB)-induced T-cell proliferation and cytokine production. SEE-induced proliferation of T cells was inhibited by monoclonal antibodies to CD2, CD11a, CD18, CD28, CD44, CD58 and ICAM-1. Anti-ICAM-1 also blocked the production of pro-inflammatory mediators, TNF alpha. and IFN gamma by SEB-stimulated T cells. These data suggest that the surface molecules, CD11a:CD18/ ICAM-1, CD2/CD58, CD28 and CD44, are all important co-receptors for T-cell activation by superantigens. Thus, like conventional antigens, multiple stimulatory signals from the interactions of these receptors are required for superantigen-induced immune responses. Reducing toxic mediators such as TNF alpha and IFN gamma by anti-ICAM antibodies in SEB-induced T-cell responses may be a useful therapeutic strategy to circumvent SEB toxicity and pathogenesis.

3/3,AB/26 (Item 26 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

05272645 References: 29
TITLE: BINDING SITES FOR BACTERIAL AND ENDOGENOUS RETROVIRAL SUPERANTIGENS CAN BE DISSOCIATED ON MAJOR HISTOCOMPATIBILITY COMPLEX CLASS II MOLECULES
AUTHOR(S): THIBODEAU J; LABRECQUE N; DENIS F; HUBER BT; SEKALY RP (Reprint)
CORPORATE SOURCE: INST RECH CLIN MONTREAL,IMMUNOL LAB,110 PINE AVE W/MONTREAL H2W 1R7/PQ/CANADA/ (Reprint); INST RECH CLIN MONTREAL,IMMUNOL LAB/MONTREAL H2W 1R7/PQ/CANADA/; UNIV MONTREAL,FAC MED,DEPT MICROBIOL & IMMUNOL/MONTREAL H3C 3J7/PQ/CANADA/; TUFTS UNIV,SCH MED,DEPT PATHOL/BOSTON//MA/02111; MCGILL UNIV,SCH MED,DEPT MICROBIOL & IMMUNOL/MONTREAL H3A 2B4/PQ/CANADA/
PUBLICATION: JOURNAL OF EXPERIMENTAL MEDICINE, 1994, V179, N3 (MAR 1), P 1029-1034
GENUINE ARTICLE#: MY484
ISSN: 0022-1007
LANGUAGE: ENGLISH DOCUMENT TYPE: NOTE

ABSTRACT: Bacterial and retroviral superantigens (SAGs) interact with major histocompatibility complex (MHC) class II molecules and stimulate T cells upon binding to the V beta portion of the T cell receptor. Whereas both types of molecules exert similar effects on T cells, they have very different primary structures. Amino acids critical for the binding of bacterial toxins to class II molecules have been identified but little is known of the molecular interactions between class II and retroviral SAGs. To determine whether both types of superantigens interact with the same

regions of MHC class II molecules, we have generated mutant HLA-DR molecules which have lost the capacity to bind three bacterial toxins (Staphylococcus **aureus** enterotoxin A [SEA], S. **aureus** enterotoxin B [SEB], and **toxic shock** syndrome toxin 1 [TSST-1]). Cells expressing these mutated class II molecules efficiently presented two retroviral SAGs (Mtv-9 and Mtv-7) to T cells while they were unable to present the bacterial SAGs. These results demonstrate that the binding sites for both types of SAGs can be dissociated.

3/3,AB/27 (Item 27 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

02966988 References: 40
TITLE: T-HELPER CELL-DEPENDENT, MICROBIAL SUPERANTIGEN-INDUCED MURINE B-CELL ACTIVATION - POLYCLONAL AND ANTIGEN-SPECIFIC ANTIBODY RESPONSES
AUTHOR(S): TUMANG JR; CHERNIACK EP; GIETL DM; COLE BC; RUSSO C; CROW MK; FRIEDMAN SM (Reprint)
CORPORATE SOURCE: CORNELL UNIV,MED CTR,NEW YORK HOSP,HOSP SPECIALSURG,COLL MED,DEPT MED,535 E 70TH ST/NEW YORK//NY/10021 (Reprint); CORNELL UNIV,MED CTR,NEW YORK HOSP,HOSP SPECIALSURG,COLL MED,DEPT MED,535 E 70TH ST/NEW YORK//NY/10021; UNIV UTAH,DEPT INTERNAL MED,DIV RHEUMATOL/SALT LAKE CITY//UT/84132
PUBLICATION: JOURNAL OF IMMUNOLOGY, 1991, V147, N2 (JUL 15), P432-438
GENUINE ARTICLE#: FX131
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Microbial superantigens (SA), bound to human B cell surface MHC class II molecules, have been shown to promote direct, "cognate" interaction with SA-reactive autologous Th cells, resulting in polyclonal Ig production. To investigate the potential for microbial SA to support Th cell-dependent, Ag-specific antibody responses, we have extended our studies to the murine system. BALB/c Th cell lines (TCL), specific for either the Mycoplasma arthritidis-derived SA or the Staphylococcus **aureus**-derived **toxic shock** syndrome toxin-1) were generated. These TCL cells are SA-specific, functionally noncross-reactive, and utilize distinct TCR V-beta gene families. Coculture of SA-reactive TCL cells and syngeneic B cells bearing the relevant SA results in B cell proliferation and polyclonal IgM and IgG production. In contrast, Ag-specific (SRBC-specific) antibody-forming cells are only generated in cultures that also contain SRBC. Thus, microbial SA-mediated Th-B cell interactions induce both polyclonal B cell activation and provide selective help for the proliferation and/or differentiation of B cells that have encountered specific Ag. In additional studies, we determined that the in vivo administration of **toxic shock** syndrome toxin-1 to young, athymic (nude) BALB/c mice results in SA binding to splenic B cells, rendering these B cells effective stimulators of and targets for SA-reactive helper TCL cells. Taken together, these results demonstrate that microbial SA mediate productive Th-B cell interactions analogous to those that occur during allospecific Th-B cell interactions in vitro and GVHD in vivo. These findings are consistent with the hypothesis that microbial SA represent environmental factors that may trigger autoimmune disease in the genetically susceptible host.

3/3,AB/28 (Item 28 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

02638915 References: 47
TITLE: STIMULATION OF THE IMMUNE SYSTEM BY MICROBIAL SUPERANTIGENS
AUTHOR(S): FLEISCHER B
CORPORATE SOURCE: UNIV MAINZ,MED 1 KLIN & POLIKLIN,PATHOPHYSIOL ABT,LANGENBECKSTR 1/D-6500 MAINZ//FED REP GER/ (Reprint)
PUBLICATION: IMMUNITAT UND INFEKTION, 1991, V19, N1 (FEB), P8-11
GENUINE ARTICLE#: FA135
LANGUAGE: GERMAN DOCUMENT TYPE: REVIEW

ABSTRACT: The enterotoxins and the **toxic-shock**-syndrome toxin-1 of Staphylococcus aureus, the erythrogenic toxins of Streptococcus pyogenes as well as a still uncharacterized exoprotein of Mycoplasma arthritidis belong to a family of exotoxins, that have in common a potent mitogenic activity for T lymphocytes of several species. These proteins stimulate CD4+- and CD8+T-lymphocytes by cross-linking the T-cell-antigen receptor with **MHC-class-II** molecules on accessory or target cells. They are functionally bivalent molecules having distinct interaction sites for variable parts of the T-cell receptor and for nonpolymorphic parts of **MHC-class-II** molecules. Due to their preferential action on T cells expressing certain V-beta-parts of the T-cell receptor the designation >>superantigens<< has been proposed. The mechanism of T-cell stimulation has apparently been conserved in evolution and has been adapted to the host's T-cell-receptor repertoire. The T cells stimulating activity apparently contributes to the pathogenesis of certain infectious diseases. Noteworthy, mice express endogenous >>superantigens<< that have similar properties.

3/3,AB/29 (Item 29 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

02545026 References: 36
TITLE: MECHANISM OF STAPHYLOCOCCUS-AUREUS EXOTOXIN A INHIBITION OF IG PRODUCTION BY HUMAN B-CELLS
AUTHOR(S): MOSELEY AB; HUSTON DP (Reprint)
CORPORATE SOURCE: BAYLOR UNIV,METHODIST HOSP,DEPT MED,MS F-501,6565 FANNIN/HOUSTON//TX/77030 (Reprint); BAYLOR UNIV,METHODIST HOSP,DEPT MED,MS F-501,6565 FANNIN/HOUSTON//TX/77030; BAYLOR UNIV,DEPT MICROBIOL & IMMUNOL/HOUSTON//TX/77030
PUBLICATION: JOURNAL OF IMMUNOLOGY, 1991, V146, N3 (FEB 1), P826-832
GENUINE ARTICLE#: EU926
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Staphylococuus enterotoxins and **toxic shock** syndrome toxin 1 are members of a family of exoproteins that are produced by staphylococci and bind specifically to MHC class II molecules. Upon binding to MHC class II molecules, these exoproteins are potent stimulators of T cell proliferation via interaction with specific TCR V-beta segments of both CD4+ and CD8+ T cells. These exoproteins also directly stimulate monocytes to secrete IL-1 and TNF-alpha. Furthermore, these exoproteins have a profound inhibitory effect on Ig production by PBMC. We examined

the effects of Staphylococcus enterotoxin A (SEA) on proliferation and Ig production of highly purified human B cells. Our results demonstrated that the binding of SEA to MHC class II molecules on B cells does not alter their ability to proliferate in response to Staphylococcus **aureus** Cowan strain I (SAC) or to produce Ig in response to SAC plus rIL-2. In contrast, the anti-DR mAb L243 inhibited both B cell proliferation and Ig production. Unable to determine a direct effect of SEA on B cell function, we investigated whether the capacity of SEA to inhibit SAC-induced Ig production by PBMC was T cell-dependent. Our results demonstrated that in the presence of T cells, under appropriate conditions, SEA can either function as a nominal Ag for stimulation of B cell proliferation and Ig production or SEA-induced Ig production required T cell help, which was dependent on pretreatment of the T cells with irradiation or mitomycin C; Ig production was not induced by SEA in the absence of T cells or in the presence of untreated T cells. Futhermore, SEA inhibited Ig production in SAC-stimulated cultures of autologous B cells and untreated T cells; pretreatment of the T cells with irradiation or mitomycin C abrogated SEA-induced inhibition of Ig production. Thus, T cell suppression of SAC-induced Ig production was dependent on T cell proliferation. Similar results were observed with both SEA and **toxic shock** syndrome toxin 1.

3/3,AB/30 (Item 30 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

02494906 References: 39
TITLE: AN EVOLUTIONARY CONSERVED MECHANISM OF T-CELL ACTIVATION BY MICROBIAL TOXINS - EVIDENCE FOR DIFFERENT AFFINITIES OF T-CELL RECEPTOR-TOXIN INTERACTION
AUTHOR(S): FLEISCHER B; GERARDYSCHAHN R; METZROTH B; CARREL S; GERLACH D; KOHLER W
CORPORATE SOURCE: UNIV MAINZ,DEPT MED 1,PATHOPHYSIOL SECT,LANGENBECKSTR 1/D-6500 MAINZ//FED REP GER/ (Reprint); LUDWIG INST CANC RES/CH-1066 EPALINGES//SWITZERLAND/; ACAD SCI GDR,CENT INST MICROBIOL & EXPTL THERAPY/DDR-6900 JENA//GER DEM REP/
PUBLICATION: JOURNAL OF IMMUNOLOGY, 1991, V146, N1 (JAN 1), P11-17
GENUINE ARTICLE#: EQ340
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: The enterotoxins produced by Staphyloccous aureus are the most potent mitogens known. They belong to a group of distantly related mitogenic toxins that differ in other biologic activities. In this study we have compared the molecular mechanisms by which these mitogens activate human T lymphocytes. We used the staphylococcal enterotoxins A to E, the staphylococcal **toxic shock** syndrome toxin, the streptococcal erythrogenic toxins A and C (scarlet fever toxins, erythrogenic toxins (ET)A, ETC), and the soluble mitogen produced by Mycoplasma arthritidis. We found that all these toxins can activate both CD4+ and CD8+ T cells and require **MHC class II** expression on accessory and target cells. However, T cells could be activated in the absence of class II molecules if the toxins ETA or SEB were co-cross-linked on beads together with anti-CD8 or anti-CD2 antibodies. Enterotoxins, **toxic shock** syndrome toxin and scarlet toxins stimulate a major fraction of human T cells, and show preferential, but not exclusive, stimulation of T

cells carrying certain TCR V-beta. In contrast, the mitogen of M. arthritidis, a pathogen for rodents stimulates only a minority of human T cells but activates a major fraction of murine T cells. Analysis of human T cell clones expressing V-beta-5 or V-beta-8 TCR showed that these clones responded also to those toxins that did not stimulate V-beta-5+ and V-beta-8+ T cells in bulk cultures. These results indicate that different TCR bind to these toxins with different affinities and that the specificity of the TCR-V-beta-toxin interaction is quantitative rather than qualitative in nature. Taken together our findings suggest that these toxins use a common mechanism of T cell activation. They are functionally bivalent proteins crosslinking **MHC class II** molecules with variable parts of the TCR. Besides V-beta, other parts of the TCR must be involved in this binding. The finding that murine T cells responded more weakly to the toxins produced by the human-pathogenic bacteria than to the Mycoplasma mitogen could indicate that the toxins have been adapted to the host's immune system in evolution.

3/3,AB/31 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01575145
Taxonomic identification of pathogenic micro-organisms and their toxic proteins
Taxonomische Identifizierung pathogener Mikroorganismen sowie ihre toxischen Proteine
Identification taxonomique de microorganisme pathogenes et de leurs proteines toxiques
PATENT ASSIGNEE:
MicroBioSystems Limited Partnership, (4224320), c/o C.T. Corp Systems, 1720 Carey Ave., Cheyenne, Wyoming 82001, (US), (Applicant designated States: all)
INVENTOR:
Powers, Linda S., 1026 Eastridge Drive, Logan, Utah 84321, (US)
Ellis, Walther R., Jr., 644 East 600 North, Apt. 26, Logan, Utah 84321, (US)
Lloyd, Christopher R., 2574 North 200 East, Logan, Utah 84341, (US)
LEGAL REPRESENTATIVE:
Bauer, Wulf, Dr. (46031), Lindenallee 43, 50968 Koln-Marienburg, (DE)
PATENT (CC, No, Kind, Date): EP 1308520 A2 030507 (Basic)
EP 1308520 A3 031112
APPLICATION (CC, No, Date): EP 2002021593 020927;
PRIORITY (CC, No, Date): US 999159 011101
DESIGNATED STATES: AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; SK; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C12Q-001/04; G01N-033/68; G01N-033/542; G01N-033/543; G01N-033/50

ABSTRACT EP 1308520 A2
The present invention describes a method for the binding of pathogenic microorganisms and their toxic proteins with ligands that have been covalently tethered at some distance from the surface of a substrate: distances of at least fifteen A are required for microorganism binding ligand tethers and at least six A are required for protein binding ligand

tethers. The ligands described herein include heme compounds, siderophores, polysaccharides, and peptides specific for toxic proteins, outer membrane proteins and conjugated lipids. Non-binding components of the solution to be analyzed are separated from the bound fraction and binding is confirmed by detection of the analyte via microscopy, fluorescence, epifluorescence, luminescence, phosphorescence, radioactivity, or optical absorbance. By patterning numerous ligands in an array on a substrate surface it is possible to taxonomically identify the microorganism by analysis of the binding pattern of the sample to the array.

ABSTRACT WORD COUNT: 143

NOTE:

Figure number on first page: 01

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200319	2011
SPEC A	(English)	200319	4767
Total word count - document A			6778
Total word count - document B			0
Total word count - documents A + B			6778

3/3,AB/32 (Item 2 from file: 348)

DIALOG(R)File 348:EUROPEAN PATENTS

01093291

Peptide T and related peptides in the treatment of inflammation, including multiple sclerosis

T-peptid und damit verwandte Peptide in der Behandlung von entzundungen einschlies slich der Multiplen Sklerose

Peptide T et peptides associes destines au traitement des inflammations, notamment la sclerose en plaques

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PATENT (CC, No, Kind, Date): EP 960886 A1 991201 (Basic)
APPLICATION (CC, No, Date): EP 99101349 930329;
PRIORITY (CC, No, Date): US 858832 920327; DK 92645 920514; US 915118 920717; US 987674 921209
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 635027 (EP 93907942)
INTERNATIONAL PATENT CLASS: C07K-005/10; C07K-014/00; A61K-038/08

ABSTRACT EP 960886 A1

Peptide T and its linear or cyclic analogues of the General Formula 1:

wherein

A is Ala, Gly, Val, Ser, Thr or absent;
B is Ala, Gly, Val, Ser, Thr or absent;
C is Ser, Thr or absent;
D is Ser, Thr, Asn, Glu, Arg, Ile, Leu or absent;
E is Ser, Thr, Asp or absent;
F is Thr, Ser, Asn, Arg, Gln, Lys, Trp or absent;
G is Tyr or absent;
H is Thr, Arg, Gly, Met, Met(O), Cys, Thr, Gly or absent;

and

I is Cys or absent;

II is Cys, an amide group, substituted amide group, an ester group or absent; at least one of the amino acids optionally being substituted by a monomeric or polymeric carbohydrate or derivative thereof, such substitution being accomplished through hydroxyl and/or amino and/or amido groups of the amino acids, comprising at least 4 amino acids, and their pharmaceutically acceptable salts, are useful in the treatment or prevention of inflammation. In particular, the peptides are useful in the treatment or prevention of multiple sclerosis, myelopathies (including HTLV-1 associate myelopathy) and symptoms and diseases associated with chronic immune activation, including chronic fatigue syndrome, **toxic shock**, arthritis, inflammatory bowel disease and host-versus-graft and graft-versus-host responses in transplant recipients.

ABSTRACT WORD COUNT: 216
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9948	362
SPEC A	(English)	9948	16432
Total word count - document A			16794
Total word count - document B			0
Total word count - documents A + B			16794

3/3,AB/33 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00584422

USE OF INTERLEUKIN-10 ANALOGS OR ANTAGONISTS TO TREAT ENDOTOXIN- OR SUPERANTIGEN INDUCED TOXICITY
VERWENDUNG VON INTERLEUKIN-10 ANALOGEN ODER ANTAGONISTEN ZUR BEHANDLUNG VON ENDOTOXIN- ODER SUPERANTIGEN INDUZIERTER TOXIZITAT
UTILISATION D'ANALOGUES OU D'ANTAGONISTES DE L'INTERLEUKINE-10 POUR TRAITER LA TOXICITE INDUITE PAR L'ENDOTOXINE OU UN SUPERANTIGENE
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LEGAL REPRESENTATIVE:
Ritter, Stephen David et al (35281), Mathys & Squire 100 Grays Inn Road, London WC1X 8AL, (GB)
PATENT (CC, No, Kind, Date): EP 600970 A1 940615 (Basic)
EP 600970 B1 991208
WO 9302693 930218
APPLICATION (CC, No, Date): EP 92917650 920806; WO 92US6378 920806
PRIORITY (CC, No, Date): US 742129 910806
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-038/00; A61K-039/395
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9949	429
CLAIMS B	(German)	9949	420
CLAIMS B	(French)	9949	477
SPEC B	(English)	9949	32967
Total word count - document A			0
Total word count - document B			34293
Total word count - documents A + B			34293

3/3,AB/34 (Item 4 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00500941
TUMOR KILLING EFFECTS OF ENTEROTOXINS AND RELATED COMPOUNDS
TUMOR-ZERSTORENDE EFFEKTE VON ENTEROTOXINEN UND VERWANDTEN VERBINDUNGEN
EFFETS DES ENTEROTOXINES ET DE COMPOSES APPARENTES POUR L'ELIMINATION DE TUMEURS
PATENT ASSIGNEE:
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PATENT (CC, No, Kind, Date): EP 511306 A1 921104 (Basic)
EP 511306 A1 930428
EP 511306 B1 020717
WO 9110680 910725
APPLICATION (CC, No, Date): EP 91903963 910117; WO 91US342 910117
PRIORITY (CC, No, Date): US 466577 900117
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
RELATED DIVISIONAL NUMBER(S) - PN (AN):
EP 1103268 (EP 2001102715)
EP 1129717 (EP 2001104586)
INTERNATIONAL PATENT CLASS: C07K-014/31; A61K-038/16
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200229	359
CLAIMS B	(German)	200229	347
CLAIMS B	(French)	200229	385
SPEC B	(English)	200229	10235
Total word count - document A			0
Total word count - document B			11326
Total word count - documents A + B			11326

3/3,AB/35 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0318203 DBR Accession No.: 2003-19343 PATENT
New vector, useful for preparing a composition for treating or preventing bacterial, viral, fungal or parasitic infection - vector-mediated gene transfer and expression in host cell for recombinant vaccine and gene therapy
AUTHOR: MCCREAVY D T; FRASER W D; GALLAGHER J A
PATENT ASSIGNEE: UNIV LIVERPOOL 2003
PATENT NUMBER: WO 200348371 PATENT DATE: 20030612 WPI ACCESSION NO.: 2003-505298 (200347)
PRIORITY APPLIC. NO.: GB 200223829 APPLIC. DATE: 20021012
NATIONAL APPLIC. NO.: WO 2002GB5512 APPLIC. DATE: 20021206
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - An vector comprising a heterologous nucleic acid sequence encoding an antigenic polypeptide and a nucleic acid molecule comprising a 3188 base pair sequence, given in the specification, a nucleic acid molecule which hybridizes to it and which encodes a protease inhibitor polypeptide, or nucleic acid molecules which comprise degenerate nucleic acid sequences. The vector is adapted for the expression of each polypeptide. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) inducing an

immune response to an antigenic polypeptide; (2) an antibody; (3) a cell transformed with the novel vector; (4) producing humanized or chimeric antibody; (5) a hybridoma cell line which produces a monoclonal antibody; (6) a vaccine comprising the novel vector; and (7) vaccinating an animal, preferably a human, against at least one pathological condition. BIOTECHNOLOGY - Preferred Vector: The vector comprises plasmid, phagemid or virus. It is provided with a nucleic acid molecule, which encodes a polypeptide that stimulates the expression of **major histocompatibility complex** (**MHC**) **class II** , where the nucleic acid consisting of:(a) a nucleic acid molecule comprising a 2030 base pair sequence; (b) a nucleic acid molecule which hybridizes to (a) and which encodes a polypeptide that stimulates **MHC class II**; or (c) nucleic acid molecules which comprise nucleic acid sequences which are degenerate because of the genetic code to the sequences. The polypeptide is CIITA (DNA Accession Number U60653). The vector is adapted for the expression of the humanized or chimeric antibodies. The viral based vector is based on viruses consisting of adenovirus, retrovirus, adeno associated virus, herpesvirus, lentivirus or baculovirus. The heterologous nucleic acid sequence encodes an antigenic polypeptide derived from a viral, bacterial, parasitic or fungal pathogen, or tumor specific antigen. The viral pathogen comprises Human Immunodeficiency Virus, Human T Cell Leukemia Virus (HTLV 1 and 2), Ebola virus, human papilloma virus (HPV), papovavirus, rhinovirus, poliovirus, herpesvirus, adenovirus, Epstein barr virus, influenza virus or influenza virus. The bacterial pathogen comprises Staphylococcus **aureus**, Staphylococcus epidermidis, Enterococcus fecalis, Mycobacterium tuberculosis, Streptococcus group B, Streptococcus pneumoniae, Helicobacter pylori, Neisseria gonorrhea, Streptococcus group A, Borrelia burgdorferi, Coccidioides immitis, Histoplasma capsulatum, Neisseria meningitidis type B, Shigella flexneri, Escherichia coli or Haemophilus influenzae. The parasitic pathogen is Trypanosoma brucei or Plasmodium. The fungal pathogen is Candida. The antigen comprises parathyroid hormone related protein, cathepsin K or prostate specific antigen. The heterologous nucleic acid molecule is controlled by its cognate promoter, or by a promoter that does not naturally control the expression of the gene from which the heterologous nucleic acid has been derived. The promoter is a constitutive promoter, derived from a gene consisting of CMV promoter, SV40, chicken beta actin, telomerase reverse transcriptase, H+/K+ ATPase or glyceraldehydes-3-phosphate dehydrogenase. The promoter is a regulatable promoter, or a cell or tissue specific promoter, derived from a gene consisting of alkaline phosphatase; albumin; casein; prostate specific antigen; osteocalcin; cathepsin K; TRAP; RankL; PC8; cytokeratins 1,6,9,10,14,16; collagen type 1; NF-ATI (NF-Atp, NF-Atc2); tyrosinase; TRP-1 or muscle specific creatine kinase. The promoter is a muscle specific promoter, derived from the gene encoding MCK or myosin light chain 3F. The protease inhibitor is an inhibitor of the proteosome. It is a mammalian or human PI31. The expression of the PI31 nucleic acid is controlled by its cognate promoter. The PI31 nucleic acid is expressed co-ordinantly with the heterologous nucleic acid. Preferred Antibody: The antibody is a diagnostic antibody. It is provided with a label or tag. It is a monoclonal antibody or its active binding fragment, humanized antibody, chimeric antibody or opsonic antibody. Preferred Vaccine: The vaccine comprises the vector and an adjuvant. Preferred Method: Inducing an immune response to an antigenic

polypeptide comprises administering to an animal, preferably a human the vector. Vaccinating an animal, preferably a human, against at least one pathological condition comprises immunizing the animal with the vector. The pathological condition is an infection caused by a virus, fungus, bacterium or parasite. The viral infection comprises AIDS, herpes, rubeola, rubella, varicella, influenza, common cold or viral meningitis. The bacterial infection comprises septicemia, tuberculosis, bacteria-associated food poisoning, blood infections, peritonitis, endocarditis, sepsis, bacterial meningitis, pneumonia, stomach ulcers, gonorrhea, strep throat, streptococcal-associated **toxic shock** , necrotizing fasciitis, impetigo, histoplasmosis, Lyme disease, gastro-enteritis, dysentery, shigellosis The pathological condition is Candidiasis. The parasitic infection comprises trypanosomiasis, malaria, schistosomiasis or Chagas disease. Producing humanized or chimeric antibody comprises: (a) providing a cell transformed or transfected with a vector which comprises a nucleic acid molecule encoding the humanized or chimeric antibody, (b) growing the cell conditions conducive to the manufacture of antibody, and (c) purifying the antibody from the cell or its growth environment. Preparing a hybridoma cell-line producing monoclonal antibodies comprises: (a) immunizing an immunocompetent mammal with the vector fusing lymphocytes of the immunized immunocompetent mammal with myeloma cells to form hybridoma cells, (b) screening monoclonal antibodies produced by the hybridoma cells of (2) for binding activity to the amino acid sequence encoded by the heterologous nucleic acid according to the invention, (c) culturing the hybridoma cells to proliferate and/or to secrete the monoclonal antibody, and (d) recovering the monoclonal antibody from the culture supernatant. ACTIVITY - Antibacterial; Virucide; Antiparasitic; Antifungal; Anti-HIV; Antiulcer. No biological data is given. MECHANISM OF ACTION - Gene therapy; Vaccine. USE - The vector is useful for preparing a composition for preventing or treating AIDS, herpes, rubeola, rubella, varicella, influenza, common cold or viral meningitis; septicemia, tuberculosis, bacteria-associated food poisoning, blood infections, peritonitis, endocarditis, sepsis, bacterial meningitis, pneumonia, stomach ulcers, gonorrhea, strep throat, streptococcal-associated **toxic shock** , necrotizing fasciitis, impetigo, histoplasmosis, Lyme disease, gastro-enteritis, dysentery or shigellosis; Candidiasis; or trypanosomiasis, malaria, schistosomiasis or Chagas disease (claimed). ADMINISTRATION - The composition is administered via oral, intravenous, intraperitoneal, intramuscular, intracavity, subcutaneous or transdermal route (claimed). No dosage is given. EXAMPLE - No relevant examples given. (52 pages)

3/3,AB/36 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0316567 DBR Accession Number: 2003-17707 PATENT
Establishing antigen-specific T cell population in host to treat diabetes, lupus by administering peptide that is presented to host thymus, resulting in positive selection of thymocytes to T cells specific for peptide - recombinant vector-mediated gene transfer and expression in host cell for use in autoimmune disease, diabetes, rheumatoid arthritis, lupus, HIV virus, pox virus, rhino virus, bacterium, fungus

infection, skin disorder and inflammation therapy
AUTHOR: IGNATOWICZ L; KRAJ P
PATENT ASSIGNEE: IGNATOWICZ L; KRAJ P 2003
PATENT NUMBER: US 20030021796 PATENT DATE: 20030130 WPI ACCESSION NO.: 2003-456280 (200343)
PRIORITY APPLIC. NO.: US 137745 APPLIC. DATE: 20020502
NATIONAL APPLIC. NO.: US 137745 APPLIC. DATE: 20020502
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - Establishing (M1) a population of antigen-specific T cells in a host, comprising administering to the host a formulation comprising a peptide through a route and in a form such that the administration results in the presentation of the peptide in the thymus of the host, where the presentation results in the positive selection of thymocytes to T cells specific for the peptide, is new.DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) assessing a test peptide for positively selecting antigen-specific CD4+ T cells in vivo, involves administering the test peptide to a mouse, where the mouse lacks substantial expression of nucleic acid sequences encoding a polypeptide such as H2-DM, invariant chain (Ii), T cell receptor-alpha (TCRalpha) or its combination, where the administration results in the presentation of the peptide in the thymus of the mouse, and assessing positively selection and maturation of primary sites to CD4+ T cells specific for the peptide; and (2) identifying (M2) a gene or gene product involved in positive selection of primary sites, involves providing a non-human mammal whose thymocytes are arrested at CD4+/CD8+, administering to the animal with a selecting peptide, obtaining a sample of mRNA from a thymocyte population at selected time following the administering of the selecting peptide, and identifying mRNA's that are present in the thymocytes population in a greater or lesser abundance than in a similar non-human mammal that has not been administered the selecting peptide. The method optionally involves providing a non-human mammal whose thymocytes are arrested at CD4+/CD8+, administering to the animal with a selecting peptide, obtaining a sample of protein from a thymocyte population at selected time following the administering of the selecting peptide, and identifying proteins that are present in the thymocytes population in a greater or lesser abundance than in a similar non-human mammal that has not been administered the selecting peptide. BIOTECHNOLOGY - Preferred Method: The thymocytes are CD3+CD4+CD8+ which mature into CD3+CD4+CD8- T cells. The peptide administered to the host comprises a T cell epitope which is specific for an antigen such as a pathogen (e.g. virus, fungus, bacteria, helminth or protozoa). Optionally, the antigen is a tumor antigen or autoantigen. Preferably, the host is screened for T cells specific for the peptide, subsequent to the administration of the peptide to the host. In (M2), the non-human animal is a mouse, to which the selecting peptide is administered intraperitoneally. The thymocyte population is obtained from fractionated or unfractionated thymus, and the sample of mRNA or protein is obtained from the thymus population 2, 4, 8, 48 or 72 hours, 4 days, 6 days, or 1 week, after the administration of the selecting peptide. The step of identifying mRNA in the thymus cell population comprises amplification, or reverse transcription of the mRNA, where the identification is carried out by hybridization of cDNA or cRNA product to a chip comprising a nucleic acid array. The step of identifying optionally comprises differential display or subtractive hybridization. The step of identifying a protein comprises two

dimensional electrophoresis, where the protein sample is labeled with one or more dyes and fluorescent signal from the resulting gel is scanned. The identifying step optionally comprises mass spectrometry or immunologic detection or protein sequencing. ACTIVITY - Antibacterial; Virucide; Fungicide; Cytostatic; Immunosuppressive; Antidiabetic; Antirheumatic; Antiarthritic; Dermatological; Antiinflammatory. MECHANISM OF ACTION - Vaccine; Induces de novo production of antigen-specific T cells. To determine if peptide selected T lymphocytes were able to mount an effective immune response in vivo the ability of peptide-selected CD4+ cells to protect mice from melanoma was assessed. Melanoma B16-F1 was transfected with constructs encoding the AbapproximatelybPCC50V54A chain tagged with yellow fluorescent protein (YFP) and Abapproximatelya chain. These transfectants weakly stimulated TCR(Tgalpha- CD4+ cells from wild-type mice. TCRTgapproximatelya-HM-2M-Ii- mice received subcutaneous injection of B16 melanoma transfectants. At the same time, half of these mice also received selecting agonist peptide. After 12 days, animals were sacrificed, and the phenotype of tumor cells and peripheral CD4+ T cells in draining lymph nodes was examined. Only mice that received selecting peptide accumulated peripheral CD4+ T cells. These cells responded to tumor as assessed by upregulation of CD69 and downregulation of CD62L. Tumors in mice that received a selecting peptide were much smaller (4-6 times) and were composed of melanoma cells without surface expression of antigenic complex (only about 1/4 of cells were YFP+ compared to more than 3/4 in mice not treated with the selecting peptide). The phenotype of peptide selected TCRTgCD4+ cells in mice with melanoma tumors was very different from peptide selected cells isolated from TCRTgapproximatelya-HM-2M-Ii- mice but not primed with melanoma cells, implying that recent thymic emigrants that left the thymus after agonist injection, become activated upon encounter with tumor cells. USE - (M1) is useful for establishing a population of antigen-specific T cells in an immunologically immature host (claimed). (M1) is useful for generating CD4+ T cells with immunosuppressive/regulatory properties that could be used for treating autoimmune diseases e.g. diabetes, rheumatoid arthritis, lupus. The method has preferred applications in newborns and small children who have highly efficient thymic selection and low number of naive peripheral T cells. The method also has applications in manipulating generation of TCR repertoire in animals of economic importance e.g. commercial animals (livestock, fish), animals of domestic importance (e.g. fish, dogs, cats, etc). The method has applications in treatment and prevention of diseases against which antigen-specific and particularly a T cell response would be effected, e.g. infections caused by viruses (human immunodeficiency virus, pox virus, rhinovirus, etc); bacterial infections caused by Streptococcus pyogenes, Staphylococcus **aureus** , Neisseria meningitidis, etc; fungal infections caused by Candida spp., Aspergillus spp., etc. The method is also useful for treating tumors, and autoimmune **diseases**, where the **T cell** selecting peptide has a tumor antigen or self-antigen epitope. ADMINISTRATION - The formulation is administered by intraperitoneal injection (claimed). Dosage of the peptide ranges from 5-100 mg/kg body weight. ADVANTAGE - The method allows the study of specificity of interaction between peptide/major histocompatibility complex (MHC) and TCR that results in positive selection, and generation of large number of positively selected cells at the same time. The method facilitates the development of antigen-specific

functional CD4+ T cells in a controlled manner. EXAMPLE - To examine the role of peptides during positive selection in vivo, transgenic mice expressing class II restricted T cell receptor (TCR) specific for analogs of a pigeon cytochrome C peptide PCC (43-58) presented by the A molecule Kraj et al., 2001 was generated. This receptor recognizes analogs of PCC(43-58) in which aspartic acid in position 50 is replaced by amino acids with neutral/hydrophobic (PCC50V (Ala-Glu-Gly-Phe-Ser-Tyr-Thr-Val-Ala-Asn-Lys-Asn-Lys-Gly-Ile-Thr), PCC50V54A (Ala-Glu-Gly-Phe-Ser-Tyr-Thr-Val-Ala-Asn-Lys-Ala-Lys-Gly-Ile-Thr), PCC46A49A50V54A (Ala-Glu-Gly-Ala-Ser-Tyr-Ala-Val-Ala-Asn-Lys-Ala-Lys-Gly-Ile-Thr), PCC50L (Ala-Glu-Gly-Phe-Ser-Tyr-Thr-Leu-Ala-Asn-Lys-Asn-Lys-Gly-Ile-Thr)) side chains. The TCR transgenic mice were backcrossed to C57BL6 TCRalpha knockout mice so that almost all T cells expressing transgenic TCR became CD4+ T cells. Initially, the capacity of agonist peptides to induce negative selection of transgenic T cells was examined. It was found that the efficiency of negative selection correlated with the potency of individual agonist peptides. However, an injection of 20 mug of any tested agonist peptide, in particular a moderate and a strong agonist (PCC50V and PCC50V54A respectively) did not induce negative selection of transgenic thymocytes as assessed by thymus cellularity, annexin V staining and TUNNEL assay. Strong agonists PCC50L and PCC50V54A induced profound negative selection when injected at 200 mug per mouse, while moderate agonist PCC50V induced only marginal deletion of CD4+ CD8+ cells. To examine the potential effect of agonist peptides on in vivo positive selection of transgenic thymocytes, the ontogeny of these cells was followed in a non-selecting thymic environment where Ab molecules were devoid of selecting peptides. The TCR(Tg)TCRalpha-mice were crossed to mice deficient in invariant chain (Ii) and H2-M to obtain TCR transgenic mice on a triple knockout background (TCR(Tg)TCRalpha-H2-M-Ii-). The development of the majority of CD4+ thymocytes is severely impaired in mice lacking H2-M and Ii molecules, two molecular chaperones that participate in peptide loading to **class II MHC** molecules Toume et al., 1997.

The thymic development of the transgenic T cells was arrested at the stage of CD4+CD8+ thymocytes and only very few transgenic CD4+ T cells were detected in the periphery. The lack of the natural positively selecting Ab/peptide complexes resulted in a block in thymocyte development and increased thymic cellularity in TCRT-gTCRapproximatelya-HM-2M-Ii- mice. Following these observations, positive selection in TCRT-gTCRapproximatelya-HM-2M-Ii- mice was restored by providing exogenous peptides. A number of irrelevant Ab-binding peptides (Asn-Ala-Asp-Phe-Lys-Thr-Pro-Ala-Thr-Leu-Thr-Val-Asp-Lys-Ala (IgGVH(59-74)), Ova(323-339), Ealpha(52-68)) and analogs of PCC (50A, 50N, 50E, 52Q) without agonist properties had no effect on thymic selection. Intraperitoneal injection of a non-deleting dose of PCC50V54A agonist peptide restored selection of CD4+ single positive thymocytes. Simultaneously, a number of CD4+8+ thymocytes upregulated CD69 and bcl-2 expression. Positive selection of D4+ thymocytes was sustained for 14 days after a single injection of the selecting peptide ligand. The cellularity of the thymus and the number of apoptotic cells detected by TUNNEL assay and annexin V staining were the same in controls and in mice injected with 20 mug of agonist peptide PCC50V54A. Four other analogs of the PCC peptide, PCC50V, PCC50L, PCC46A49A50V54A and PCC50F54A, injected at the same dose (20 mug), also restored positive selection of transgenic thymocytes. These results proved that positive selection of CD4+ T cells was induced in vivo by different

agonist ligands. An injection of soluble agonist into TCRT-gTCRapproximatelya-HM-2M-Ii- radiation chimeras also resulted in positive selection of transgenic CD4+ T cells, despite the expression of wild-type Ab/peptide complexes on bone marrow derived thymic stromal cells. (48 pages)

Set	Items	Description
S4	4604	AU=(BROWN, E? OR BROWN E?)
S5	5677	AU=(LEE, L? OR LEE L?)
S6	340	AU=(HOOK, M? OR HOOK M?)
S7	6	S4 AND S5 AND S6
S8	30	S4 AND (S5 OR S6)
S9	6	S5 AND S6
S10	4	(S8 OR S4 OR S5 OR S6) AND S1
S11	8	(S7 OR S9 OR S10) NOT S2
S12	4	RD (unique items)

- Author (S)

>>>No matching display code(s) found in file(s): 65, 113

12/3,AB/1 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

16711932 Document Delivery Available: 000184658800065 References: 38
TITLE: Decorin-binding sites in the adhesin DbpA from Borrelia burgdorferi - A synthetic peptide approach
AUTHOR(S): Pikas DS; **Brown EL**; Gurusiddappa S; **Lee LY**; Xu Y; **Hook M (REPRINT)**
AUTHOR(S) E-MAIL: mhook@ibt.tamu.edu
CORPORATE SOURCE: Texas A&M Univ, Ctr Extracellular Matrix Biol, 2121 W Holcombe Blvd/Houston//TX/77030 (REPRINT); Texas A&M Univ, Ctr Extracellular Matrix Biol, /Houston//TX/77030
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF BIOLOGICAL CHEMISTRY, 2003, V278, N33 (AUG 15), P 30920-30926
GENUINE ARTICLE#: 710AN
PUBLISHER: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA
ISSN: 0021-9258
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Lyme disease is caused by the spirochete Borrelia burgdorferi following transmission from infected Ixodes ticks to human hosts. Following colonization of the skin, spirochetes can disseminate throughout the body, resulting in complications that can include ocular, cardiac, neural, and skeletal disease. We have previously shown that B. burgdorferi expresses two closely related decorin-binding adhesins (DbpA and DbpB) of the MSCRAMM (microbial surface component recognizing adhesive matrix molecule) type that can mediate bacterial attachment to extracellular matrices in the host. Furthermore, three Lys residues in DbpA appear to be critical for the binding of DbpA to decorin. We have now characterized the interaction of DbpA and decorin further by using a synthetic peptide approach. We synthesized a panel of peptides that spanned the DbpA sequence and examined their ability to inhibit the binding of intact DbpA to decorin. From these studies, we identified a decorin-binding peptide that lost this activity if the sequence was either scrambled or if a critical Lys residue was chemically modified. A minimal decorin-binding peptide was identified by

examining a set of truncated peptides. One peptide is proposed to contain the primary decorin-binding site in DbpA. By comparing the amino acid sequences of 29 different DbpA homologs from different B. burgdorferi sensu lato isolates, we discovered that the identified decorin-binding sequence was quite variable. Therefore, we synthesized a new panel of peptides containing the putative decorin-binding sequence of the different DbpA homologs. All of these peptides were active in our decorin-binding assay, and consensus decorin binding motifs are discussed.

12/3,AB/2 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

15116109 Document Delivery Available: 000179377000013 References: 70
TITLE: The Staphylococcus aureus Map protein is an immunomodulator that interferes with T cell-mediated responses
AUTHOR(S): **Lee LY**; Miyamoto YJ; McIntyre BW; **Hook M**; McCrea KW; McDevitt D; **Brown EL (REPRINT)**
AUTHOR(S) E-MAIL: ebrown@ibt.tamu.edu
CORPORATE SOURCE: Texas A&M Univ Syst, Ctr Extracellular Matrix Biol, 2121 W Holcombe Blvd,Suite 603/Houston//TX/77030 (REPRINT); Texas A&M Univ Syst, Ctr Extracellular Matrix Biol, /Houston//TX/77030; Univ Texas, Dept Immunol, /Houston//TX/77030
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF CLINICAL INVESTIGATION, 2002, V110, N10 (NOV), P 1461-1471
GENUINE ARTICLE#: 617TM
PUBLISHER: AMER SOC CLINICAL INVESTIGATION INC, 35 RESEARCH DR, STE 300, ANN ARBOR, MI 48103 USA
ISSN: 0021-9738
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Staphylococcus aureus (SA) is an opportunistic pathogen that affects a variety of organ systems and is responsible for many diseases worldwide. SA express an **MHC class II** analog protein (Map), which may potentiate SA survival by modulating host immunity. We tested this hypothesis in mice by generating Map-deficient SA (Map-SA) and comparing disease outcome to wild-type Map SA-infected mice. Map-SA-infected mice presented with significantly reduced levels of arthritis, osteomyelitis, and abscess formation compared with control animals. Furthermore, Map-SA-infected nude mice developed arthritis and osteomyelitis to a severity similar to Map(+)SA-infected controls, suggesting that T cells can affect disease outcome following SA infection and Map may attenuate cellular immunity against SA. The capacity of Map to alter T cell function was tested more specifically in vitro and in vivo using native and recombinant forms of Map. T cells or mice treated with recombinant Map had reduced T cell proliferative responses and a significantly reduced delayed-type hypersensitivity response to challenge antigen, respectively. These data suggest a role for Map as an immunomodulatory protein that may play a role in persistent SA infections by affecting protective cellular immunity.

12/3,AB/3 (Item 3 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

06726440 References: 26
TITLE: STAPHYLOCOCCUS AUREUS EXPRESSES A **MAJOR HISTOCOMPATIBILITY COMPLEX CLASS II** ANALOG
AUTHOR(S): JONSSON K; MCDEVITT D; MCGAVIN MH; PATTI JM; **HOOK M (Reprint)**
CORPORATE SOURCE: TEXAS A&M UNIV,INST BIOSCI & TECHNOL,DEPT BIOCHEM & BIOPHYS,2121 W HOLCOMBE BLVD/HOUSTON//TX/77030 (Reprint); TEXAS A&M UNIV,INST BIOSCI & TECHNOL,DEPT BIOCHEM & BIOPHYS/HOUSTON//TX/77030; TEXAS A&M UNIV,CTR EXTRACELLULAR MATRIX BIOL/HOUSTON//TX/77030; UNIV MANITOBA/WINNIPEG/MB R3E 0W2/CANADA/
PUBLICATION: JOURNAL OF BIOLOGICAL CHEMISTRY, 1995, V270, N37 (SEP 15), P 21457-21460
GENUINE ARTICLE#: RU757
ISSN: 0021-9258
LANGUAGE: ENGLISH DOCUMENT TYPE: NOTE

ABSTRACT: Staphylococcus aureus expresses various surface proteins which specifically recognize and bind to different host molecules. We have previously identified a bacterial protein that exhibits a broad specificity and binds to several mammalian extracellular proteins. The gene encoding this bacterial component has now been cloned and sequenced. The deduced protein consists predominantly of six repeated domains of 110 residues. Each of the repeated domains contain a subdomain of 31 residues that share striking sequence homology with a segment in the peptide binding groove of the beta chain of the **major histocompatibility complex** (**MHC**) **class II** proteins from different mammalian species.
The purified recombinant bacterial protein bound several mammalian proteins, including recombinant osteopontin, suggesting a protein-protein interaction and also specifically recognized a 15 amino acid residue synthetic peptide. Taken together, these results suggest that the bacterial protein resembles mammalian **MHC class II** molecules with respect to both sequence similarities and peptide binding capabilities.

12/3,AB/4 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01509469
METHOD OF PREVENTING T CELL-MEDIATED RESPONSES BY THE USE OF THE **MAJOR HISTOCOMPATIBILITY COMPLEX CLASS II** ANALOG PROTEIN (MAP PROTEIN) FROM STAPHYLOCOCCUS **AUREUS**
VERFAHREN ZUR PRAVENTION VON T-ZELLEN-VERMITTELTEN REAKTIONEN DURCH VERWENDUNG DES MAP-PROTEINS (HAUPTHISTOKOMPATIBILITATSKOMPLEX KLASSE II ANALOGES PROTEIN) AUS STAPHYLOCOCCUS AUREUS
METHODES DESTINEES A PREVENIR LES REPONSES INDUITES PAR LES LYMPHOCYTES T AU MOYEN D'UNE PROTEINE ANALOGUE DE CLASSE II A COMPLEXE MAJEUR D'HISTOCOMPATIBILITE (PROTEINE MAP) ISSUE DE I STAPHYLOCOCCUS AUREUS /I

PATENT ASSIGNEE:
THE TEXAS A&M UNIVERSITY SYSTEM, (421778), 310 Wisenbaker,, College Station, TX 77843-3369, (US), (Applicant designated States: all)
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LEGAL REPRESENTATIVE:
Cripps, Joanna Elizabeth et al (89381), Mewburn Ellis York House 23 Kingsway, London WC2B 6HP, (GB)
PATENT (CC, No, Kind, Date): EP 1355662 A2 031029 (Basic)
WO 2002077010 021003
APPLICATION (CC, No, Date): EP 2002736474 020110; WO 2002US401 020110
PRIORITY (CC, No, Date): US 260523 P 010110
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A61K-039/00; A61K-039/02; A61K-039/085
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
? log y
30apr04 15:05:31 User219783 Session D2013.3